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Cities and mental health

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Cities and mental health

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Editorial: Cities and mental health

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KEYWORDS

cities, urban, mental health, wellbeing, greenspace, urban planning

Editorial on the Research Topic
Cities and mental health

The link between urbanization and mental health is multifaceted and draws considerable attention from researchers and professionals worldwide. The Research Topic "Cities and Mental Health" dives into this theme, illuminating the influences of urban living on mental health and some possible causal pathways. Specifically, this editorial investigates the complexity of the relationship between urbanization and mental health, highlighting the increased interest among scholars and practitioners around the world. Here we present an overview of current studies by synthesizing twelve research articles published in the Research Topic. The majority of these studies are centered on China, followed by two studies from Germany, two from Taiwan and one from Portugal. According to the word analysis conducted with Nvivo 12 Pro software that visualizes the 1,000 most frequent words retrieved from the published articles, terms: "social" "health" and "urban" are the most frequently used by the authors. In Figure 1 we show the results of the word analysis in a form of a word-cloud.

The social aspects of urban life emerge as critical determinants of mental health. One study in the collection associates perceived social cohesion with depressive symptoms among internal migrants in China, with social adaptation acting as a mediator (Qu et al.). In it, authors demonstrate that fostering social cohesion and promoting social strategies can help alleviate the mental health disparities among this vulnerable population, as well as highlighting the especially vulnerable group of involuntary rural-to-urban migrants, who may require additional social support. Furthermore, the impact of housing tenure mix on mental health is examined in the megacity of Guangzhou, China, revealing that while there is no direct impact, social participation mediates the decrease in depressive symptoms (Zhang et al.).

Moving into family dynamics, a paper from Changsha, the capital of Hunan province, reports increasing trends of various mental health problems among Chinese adolescents in urban areas between 2016 and 2020, emphasizing the urgency to address mental health issues in cities, especially among younger demographics (Wu et al.). Another article explores the protective role of good family functioning against adolescent delinquency in another Chinese megacity (Wan et al.). The authors highlight the value of positive behavior recognition in family environments, which is relevant in both urban and rural settings.

Socioeconomic aspects in urban settings also show significant influence on mental health through the issue of perceived stigma as presented by Hohmann et al. in a German study . In it, the authors imply a need for targeted interventions and public education programs that take into account the varying social environments in urban areas to reduce stigma.

A contribution from Ancora and colleagues titled "C*ities and neuroscience research: a systematic literature review*" helps establish the broader background by investigating the neural mechanisms underlying cognitive and emotional processes in relation to urban environment exposure (Ancora et al.). The paper recommends policy-making for healthier and sustainable cities, emphasizing the considerable mental benefits of green spaces and urban upbringing with high nature exposure as well as the role of air pollution in neurodegenerative process and cognitive decline.

Further down this path, the influence of city environments on psychiatric disease development is tackled by a German study that explores the prevalence of neural autoantibodies in urban vs. rural psychiatric patients (Hansen et al.). The paper concludes that, while there were no significant findings in antibodies levels between rural and urban patients, more extensive studies are needed to explore the possible higher prevalence of autoimmune-related psychiatric syndromes in larger cities.

The urban soundscape's influence on mental health is broached by a Taiwanese study, reporting on significant associations between road traffic noise at specific frequencies and increased depression prevalence, even when controlling for the effects of pollution

FIGURE 1
Word cloud generated by Nvivo 12 Pro illustrating the 1,000 most frequent words extracted from the analysis of 12 articles. The terms "social" and "health" dominate the center of the image, indicating their significant prevalence within the dataset.

(Lin et al.). In another Taiwanese study the effects of natural environments on mental health are brought to light in a context of creativity in a study titled "The influence of natural environments on creativity" (Yeh et al.). The authors argue that viewing natural environments fosters flexibility and imagination, highlighting another dimension of how urban greening can influence productivity and wellbeing.

Following the research on sensory stimuli influencing the mental health Chinese meta-analysis by Tan and colleagues summarized the existing clinical trials on the essential oils in treatment of psychiatric disorders (Tan et al.). It concludes that natural scents of lemon and lavender showed to be the most effective in treatment of anxiety.

An important aspect touched upon by this Research Topic is the mental health of urban professionals and their productivity, with two papers investigating these issues. One paper documents higher depression prevalence among medical staff in Hainan, China, associating it with anxiety, sleep disorders, and job-related stressors (Lu et al.). In contrast, another study reveals that planned urbanization can improve mental health among middle-aged and older adults in China by promoting social participation and improving living conditions (Hong et al.). This dichotomy underscores the nuanced impacts of urban life on mental wellbeing, depending on one's occupation and socioeconomic status.

In conclusion, these papers collectively underscore the significant interplay between urban environments and mental health. The findings affirm the imperative to consider multifaceted factors including environmental, social, and economic aspects in urban planning and health policy-making, and as a whole show commonalities across urban areas in different countries. While a lot of research is yet to be done to identify positive interventions, the effect of natural environments, multi-sensory exposure, and participatory approaches at the neighborhood levels seem to be the most promising tools to alleviate the burden of mental health in cities while promoting productivity and creativity. This collection of studies prompts researchers and policymakers to discuss and work together toward healthier, greener and more supportive cities for better mental health outcomes.

Author contributions

AO-G: Conceptualization, Writing—original draft, Writing—review and editing. AR: Visualization, Writing—review and editing. ACR: Writing—review and editing. SK: Writing—review and editing. BM: Writing—review and editing. NT: Writing—review and editing. RH: Writing—review and editing.

Conflict of interest

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Publisher's note

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BRIEF RESEARCH REPORT
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Increasing Trends in Mental Health Problems Among Urban Chinese Adolescents: Results From Repeated Cross-Sectional Data in Changsha 2016–2020

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This study performed a repeated cross-sectional analysis to explore possible trends in mental health problems among Chinese adolescents over the years of 2016–2020. A total of 2,837 different seventh-grade students were surveyed in three waves from a junior high school in Changsha city, Hunan province in China (978 in 2016, 949 in 2019, and 910 in 2020) using the Mental Health Inventory of Middle School Students (MMHI-60). The results showed that obsessive-compulsive tendencies, interpersonal sensitivity, depression, anxiety, academic stress, and emotional disturbance problems were significantly increased in surveyed adolescents from 2016 to 2020. Moreover, positive rates of most of these problems were significantly higher in females than males, and were significantly increased in only females. These results highlight the importance of focusing on mental health problems among urban Chinese adolescents, especially among girls.

Keywords: mental health, adolescents, depression, anxiety, sex difference

INTRODUCTION

Childhood and early adolescence are crucial periods for mental health development with a particularly high risk for mental health problems (1, 2). These problems can persist into adulthood and even lead to serious mental diseases if they are undetected or not treated appropriately (3–5).

Over the past decades, China has witnessed great developments in economy and society (6). However, in contrast to the increase in economy, multiple studies have reported a dramatic decrease in mental health in China, especially in Chinese adolescents during the same period (6–9). For example, a recent cross-temporal meta-analysis showed that Chinese adolescents' depression was significantly increased from 1989 to 2018 (7). Another cross-temporal meta-analysis, which was based on data between 1992 and 2017, also reported that Chinese adolescents' anxiety level was significantly increased since 1992 (8). To improve public mental health, it is thus important to assess the prevalence and changes over time in the prevalence of mental health problems in Chinese adolescents (7).

Although having gained important insights into trends in mental health problems in Chinese adolescents in recent years, the above-mentioned published literatures are limited in several ways. First, almost all these studies were based on data before the year 2018, and reports on newly trends after that time point are sparse. Second, most of them only focused on a single dimension of mental health such as depression or anxiety symptoms, while a more comprehensive survey in multiple dimensions is rare. Third, most of these studies are cross-temporal meta-analyses, which pooled previous studies using the same mental health assessing instruments [e.g., Self-rating Depression Scale (7)] together. However, such an approach may not be able to fully address the potential bias caused by regional diversity [e.g., the pooled studies were across different provinces in China with different economic and educational levels (7)].

In this study, we performed a repeated cross-sectional analysis to overcome the above limitations. Repeated cross-sectional studies utilize the same instruments and methodologies in the same population over multiple time timepoints; therefore, they were thought to be most suitable for investigating trends of mental health statuses over time (10, 11). In specific, a total of 2,837 different urban adolescents from a sample high school in Changsha city, Hunan province in China were surveyed in three waves from 2016 to 2020. Mental health status was assessed using a validated multi-dimensional mental health scale, Mental Health Inventory of Middle School Students (MMHI-60) (12, 13) and compared between different years.

METHODS

This study uses data collected from 2016 to 2020 in a total of 2,837 different urban Chinese junior high school students in three waves (978 students in September 2016; 949 students in September 2019; and 910 students in September 2020). Note that all participants were new seventh-grade students when they completed the survey, and all students were from the same campus of a high school (Tianding campus of The High School Attached to Hunan Normal University and Bocai Experimental School in Changsha city, Hunan province, China). A total of 76 participants (46 males and 30 females) with missing data for any item of the MMHI-60 in the surveys have been excluded from the study; there was no significant difference in sex ratio or age between the excluded participants and included participants in any wave (Chi-square test or t-test, $p > 0.05$). All participants and their supervisors provided written informed consents and the study was approved by the Ethics Committees of the Second Xiangya Hospital of Central South University, Changsha (IRB Number: 2021015).

All participants completed the MMHI-60 in the classroom to assess their mental health statuses. MMHI-60 is a validated and widely used self-report measure of mental health problems, which includes 10 subscales of distinct dimensions (60 items in total, and 6 items for each subscale): obsessive-compulsive tendencies, paranoid ideation, hostility, interpersonal sensitivity, depression, anxiety, academic stress, maladaptation, emotional disturbance and psychological imbalance (12–16). All items were scored from 1 to 5, and higher scores indicate more severe mental health problems. According to Wang et al. (13), a cutoff of average points of a subscale ≥ 2 is identified as having a mental health problem (positive for that subscale). This cutoff has shown good specificity and sensitivity in previous research (14, 15, 17). Positive rates of each subscale were calculated based on such a cutoff.

Differences in the sex ratio of participants between different waves were compared using the Chi-square test. Referring to previously published studies (18, 19), the Cochran–Armitage trend tests were used to determine if there are increasing or decreasing linear time trends of all MMHI-60 subscales' positive rates from 2016 to 2020. Moreover, considering that sex differences in mental health among adolescents have been widely reported (11, 14, 20), positive rates of all subscales were further compared between males and females using the Chi-square test; the significances of time trends in positive rates were also tested in males and females separately using the Cochran–Armitage trend tests. All statistical significances were set at $p < 0.05$.

TABLE 1 | Sample characteristics of the participants surveyed in each wave.

	Wave 1 (September 2016, $n = 978$)	Wave 2 (September 2019, $n = 949$)	Wave 3 (September 2020, $n = 910$)	Statistics
Sex (male/female)	544/434	503/446	481/429	$\chi^2 = 1.873$, $p = 0.392$
Age (years)	Unavailable	12.027 ± 0.432	Unavailable	/
MMHI-60 results (positive/negative/positive rate)				
Obsessive–compulsive tendencies	484/494/49.5%	596/353/62.8%	605/305/66.5%	$z = 7.566$, $p < 0.001$
Paranoid ideation	274/704/28.0%	272/677/28.7%	257/653/28.2%	$z = 0.115$, $p = 0.909$
Hostility	257/721/26.3%	265/684/27.9%	247/663/27.1%	$z = 0.437$, $p = 0.662$
Interpersonal sensitivity	305/673/31.2%	326/623/34.4%	332/578/36.5%	$z = 2.435$, $p = 0.015$
Depression	254/724/26.0%	294/655/31.0%	322/588/35.4%	$z = 4.437$, $p < 0.001$
Anxiety	354/624/36.2%	367/582/38.7%	396/514/43.5%	$z = 3.241$, $p = 0.001$
Academic stress	348/630/35.6%	362/587/38.2%	392/518/43.1%	$z = 3.326$, $p < 0.001$
Maladaptation	209/769/21.4%	235/714/24.8%	224/686/24.6%	$z = 1.683$, $p = 0.092$
Emotional disturbance	338/640/34.6%	350/599/36.9%	370/540/40.7%	$z = 2.731$, $p = 0.006$
Psychological imbalance	167/811/17.1%	168/781/17.7%	184/726/20.2%	$z = 1.753$, $p = 0.080$

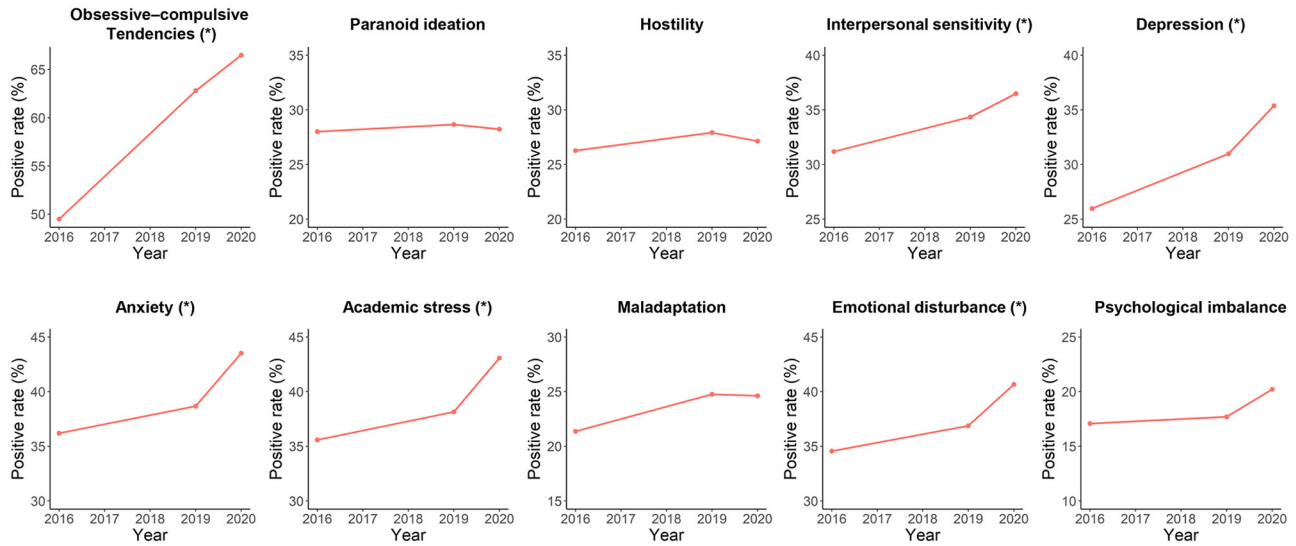

FIGURE 1 | Trends in positive rates of each mental health problem in surveyed participants during the period of 2016–2020. The "*" indicates a significant increasing trend with $p < 0.05$.

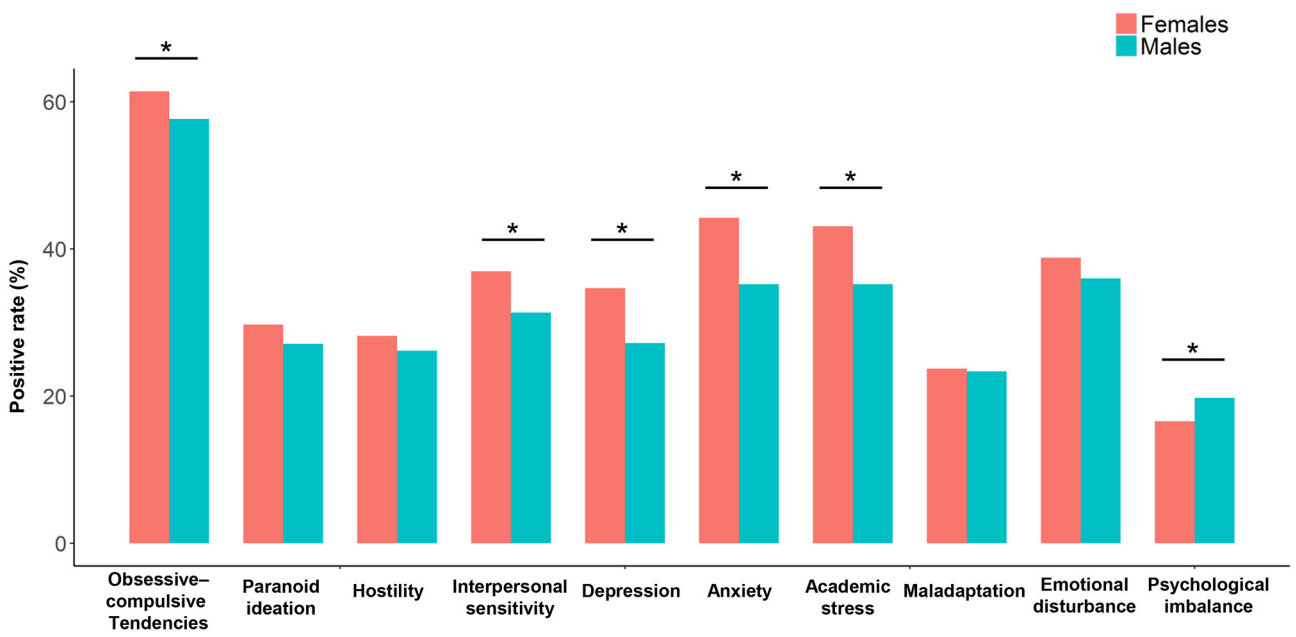

FIGURE 2 | Comparisons on positive rates of each mental health problem between the female and male participants. The "*" indicates a significant sex difference with $p < 0.05$.

RESULTS

Demographic and mental health characteristics of students in each wave were shown in **Table 1**. There was no significant difference in sex ratio among the three waves ($\chi^2 = 1.873$, $p = 0.392$). Data on participants' age was only available for the second wave and could not be compared. Cochran-Armitage trend tests showed that positive rates of the obsessive-compulsive tendencies ($p < 0.001$), interpersonal sensitivity ($p = 0.015$), depression ($p < 0.001$), anxiety ($p = 0.001$), academic stress ($p < 0.001$) and emotional disturbance ($p = 0.006$) problems were significantly increased during the period of 2016 to 2020, while no significant increasing or decreasing trends were found in positive rates of the paranoid ideation, hostility, maladaptation and psychological imbalance problems (all $p > 0.05$). The trends in positive rates of each mental health problem were also visualized in **Figure 1**.

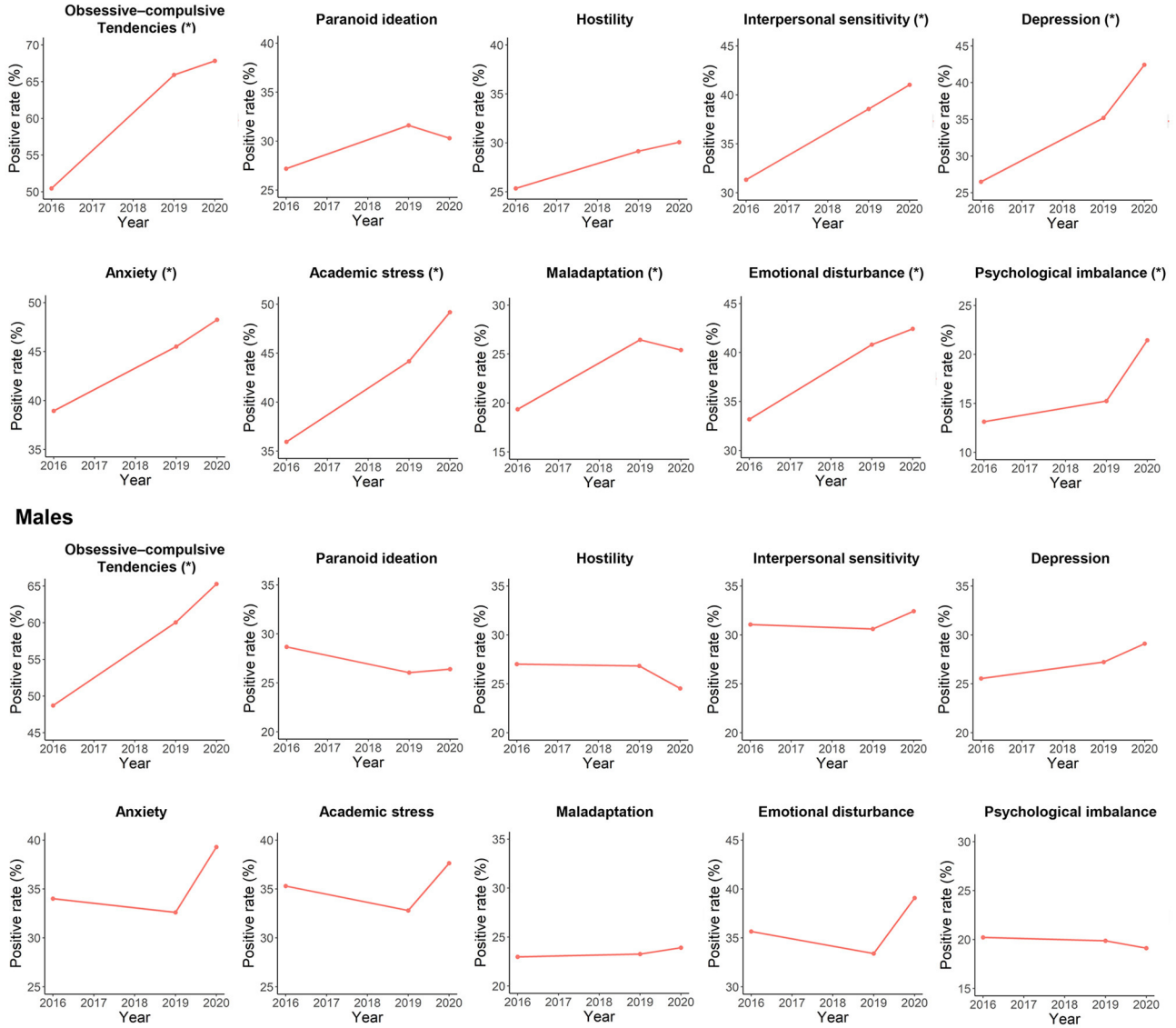

FIGURE 3 | Trends in positive rates of each mental health problem during the period of 2016–2020 in surveyed females and males, respectively. The "*" indicates a significant increasing trend with $p < 0.05$.

The females had significantly higher positive rates of obsessive-compulsive tendencies, interpersonal sensitivity, depression, anxiety, and academic stress, but a significantly lower positive rate of psychological imbalance than males (**Figure 2**; **Supplementary Table 1**). From 2016 to 2020, the positive rate of obsessive-compulsive tendencies was significantly increased in both males and females, while positive rates of interpersonal sensitivity, depression, anxiety, academic stress, maladaptation, emotional disturbance, and psychological imbalance were significantly increased in only females (**Figure 3**; **Supplementary Tables 2–3**).

DISCUSSION

In this study, we performed a repeated cross-sectional analysis to explore the possible trends in mental health problems among Chinese adolescents over the years of 2016–2020. Compared with most published studies for similar purposes, we had advantages in methodologies (uniformity of surveyed populations) and data timeliness (until the most recent years).

Our results showed that positive rates of multiple mental health problems including obsessive-compulsive tendencies, interpersonal sensitivity, depression, anxiety, academic stress,

and emotional disturbance problems were all significantly increased from September 2016 to September 2020 in surveyed participants (**Figure 1**). Some previous studies have reported similar trends of increasing mental health problems in Chinese adolescents; however, all these studies were based on data before the year 2018 (6–9). Thus, as a supplement to these studies, our study suggests the possibility that mental health in Chinese adolescents could have been deteriorating in the most recent years. The increases in mental health problems, as discussed in some previous studies, may be associated with the reported changes in several social and psychological factors in recent years in China [e.g., increasing divorce rate (21)]. It is noteworthy that the COVID-19 outbreak in 2020, which has been widely reported to have negative mental effects on the worldwide population (22–25). For instance, due to school closures and social isolation, adolescents may experience losses of close peer relationships during the pandemic which can lead to depression and anxiety (26, 27). Therefore, the pandemic-related effects may also play an important role in these trends besides other factors.

Further analyses showed that positive rates of most of the above mental health problems were significantly higher in females than males and were significantly increased in only females during 2016–2020. Although being somewhat surprising, similar results have been reported among adolescents in other countries that compared with boys, girls may be more affected by mental problems (28–30). There are multiple biological and social factors which might account for such sex differences. For example, adolescent girls are more likely than males to engage in social behaviors which exacerbate depressive symptoms in response to stresses (28, 31). Together, our results highlight the importance of focusing on mental health problems among urban Chinese adolescents, especially among girls.

It is notable that in our study, positive rates of some mental health problems were relatively high compared with results of several other studies in Chinese adolescents. For example, the prevalence of anxiety symptoms in 2020 was 43.5% in our sample, but only 37.4% (32) and 19% (26) in two other studies, respectively. Such difference may be partly attributed to the different scales used [e.g., the 7-item Generalized Anxiety Disorder scale to assess anxiety (26, 33)]. Using different scales may change the positive rates, which should be noted when comparing our results with those of other studies.

Our study has several limitations. First, this survey was not performed in the years 2017 and 2018. Second, data on age was lacking for most participants. However, since children were required to enter school until 6 years old in China (34), all participants should had a close age around 12 when they were surveyed. Third, we used Cochran-Armitage trend test based on the assumption that trends in all mental health problems are linear; however, the trends may also be non-linear. Lastly, the survey was performed in only a single school in an urban area (Changsha city), and only seventh-grade students in early adolescence. Thus, it should be cautious to interpret our results as trends in nationwide populations. Further studies conducted in a larger sample, in wider regions including rural areas, and in a wider range of age would be necessary to expand our knowledge in mental health among Chinese adolescents.

CONCLUSION

In conclusion, in this study, we found that positive rates of multiple mental health problems were significantly increased during 2016–2020 in a group of surveyed adolescents in Changsha city, China. Moreover, positive rates of most of these problems were found to be significantly higher in females than males, and significantly increased during 2016–2020 in only females. Such results highlight the importance of focusing on mental health problems among Chinese adolescents, especially among girls.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Second Xiangya Hospital of Central South University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

ZW, XC, ZZ, and YL conceived the idea, designed the study, collected and analyzed the data, drafted, and approved the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.829674/full#supplementary-material

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City Environment and Occurrence of Neural Autoantibodies in Psychiatric Patients

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Background: City living might lead to a higher risk of psychiatric disease, but to date there is no evidence of any correlation between an urban environment and the occurrence of neural autoantibodies in psychiatric disease. Our aim is to identify whether the number of patients with and without neural autoantibodies living in diverse rural and urban environments differ.

Methods: We enrolled retrospectively a cohort of 167 psychiatric patients *via* a cross-sectional design from the Department of Psychiatry and Psychotherapy University Medical Center Göttingen and determined serum and/or CSF neural autoantibodies in them. The patients live in the German states of Lower Saxony, Thuringia, and Hessen. Their data were investigated in conjunction with the location of their primary residence. We categorized them into five different categories depending upon their primary residence: one rural and four different urban environments depending on their population numbers.

Results: We identified 36 psychiatric patients with neural autoantibodies, and 131 psychiatric patients with none. In total, 24 psychiatric patients with neural autoantibodies were classified as sharing a possible, probable, or definitive autoimmune origin according to our recently set criteria. We observed as a non-significant trend that more psychiatric patients with neural autoantibodies and a probable or definitive autoimmune origin (45.8%) live in a major city with over 100,000 inhabitants than do psychiatric patients presenting no evidence of autoantibodies (26.4%). However, we identified no relevant differences between (1) psychiatric patients with and without neural autoantibodies or between (2) psychiatric patients with a possible, probable, or definitive autoimmune origin and those without such autoantibodies in relation to the diverse rural and urban environmental settings.

Conclusion: The inherently different aspects of rural and urban environments do not appear to be relevant in determining the frequency of neural autoantibodies in psychiatric

patients in Lower Saxony, Thuringia, and Hessen in Germany. Furthermore, large-scale studies involving other states across Germany should be conducted to exclude any regional differences and to examine the tendency of a higher frequency in large cities of autoimmune-mediated psychiatric syndromes.

Keywords: urban environment, major city, autoimmunity, psychiatry, neuronal autoantibodies

INTRODUCTION

Psychiatric diseases have multifactorial causes. Genetic and environmental factors interact together with the patient's individual life events that might result in the manifestation of psychiatric symptoms and potentially culminate in a psychiatric disorder. A recent investigation in a large biobank cohort of 385,793 participants in the United Kingdom showed that a subject's primary residence can be determined by their genetic risk of psychiatric disease (1). Their study indicates that a subject's genes are influenced by their environment, which in turn determine an individual's risk for psychiatric disease. Thus, whether the location of someone's primary residence, being urban or rural, raises that person's risk for psychiatric disease depends on their specific genes. In other words, the manifestation of psychiatric disease in its specific urban or rural environment is to some extent genetically determined. Beyond the role that genes play, there is ample evidence that humans react to stress differently according to environmental conditions. The amygdala is a brain structure involved in processing stress. Another study showed that the amygdalas of humans living in an urban environment are more active (2), inducing elevated amygdala-related stress processing in humans in an urban environment. And it is not just the amygdala that is known to be involved in such stress processing in humans in an urban environment, as the same working group (2) demonstrated that social stress processing within the perigenual anterior cingulate cortex is also associated with growing up in a city. The amygdala is known to be involved in the autoantibody-mediated disease of the central nervous system, such as autoimmune encephalitis (3). Thus, it is tempting to speculate that an autoantibody-driven inflammation of the amygdala would be much more active in an urban area through stress processing combined with inflammation, which would thereby facilitate the induction or exaggeration of emotional states in psychiatric patients leading to hospital admission. These studies demonstrate that living in an urban environment can alter the conditions that induce psychiatric symptoms and even psychiatric disease. However, we do not yet know whether the neural autoantibodies that play a growing role in specific subtypes of the psychiatric disease are also influenced by such environmental factors. Several recently developed criteria serve to classify psychiatric patients with neural autoantibodies into those that might have an autoimmune origin (4) that often differ from non-organic psychotic disorders with other pathomechanisms responsible for generating disease. There are other criteria to define autoimmune encephalitis (5) in which psychiatric symptoms are potentially a relevant component or even the main phenotype, as described in a study by Endres et al. (6). A recent study (7) demonstrated a higher seroprevalence of glutamic acid decarboxylase 65 (GAD65) autoantibodies in African humans in a rural environment. Rural and city environments in Africa and Europe are extremely diverse (due to the degree of industrialization, cultural factors, etc.), which makes such research findings difficult to apply to industrial environmental conditions in more advanced industrial cultures. GAD65 antibodies are more frequently detected in rural Ghana populations; they are mainly influenced by the presence of fever, and the patient's medical history, i.e., fevers and higher liver enzyme concentrations (7). Reasons for these factors are unknown, but might be attributable to less available medical care in rural than in urban Ghana populations. These conditions are absent in Europe and other industrialized cultures where adequate medical care is available in both rural and urban locations. Nevertheless, the serum prevalence of neural autoantibodies in psychiatric patients might be determined by environmental factors, such as specific population-based viruses, which spread more extensively in cities, and eventually might cause neural autoantibodies to be produced as an automatic autoimmune process following severe viral infection, as depicted in a study (8) with increased neural autoantibodies in patients with COVID-19 with neuropsychiatric symptoms. Several non-pathogenic microorganisms that regularly induce immune reactions might lead to less autoimmune disease, as the immune system is better trained to distinguish pathogenic from non-pathogenic antigens. Based on these hypothetical reflections, our hypothesis is—in an urban environment—to detect a higher frequency of psychiatric patients presenting neural autoantibodies than psychiatric patients without neural autoantibodies. Our investigation's objective is to assess the occurrence vs. non-occurrence of autoantibodies in psychiatric patients in urban and rural populations.

MATERIALS AND METHODS

We retrospectively enrolled a study cohort of 167 psychiatric patients with diagnosis classes from F00–F69 according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD10 system) from the Department of Psychiatry and Psychotherapy University Medical Center Göttingen between 2017 and 2020 in which we determined serum and/or cerebrospinal (CSF) neural autoantibodies analyzed in the Euroimmun laboratory in Lübeck. We screened these patients for autoantibodies for differential-diagnostic reasons. Our patient cohort's (n = 167 patients) data was sourced from patient files exclusively from the in- and outpatient Department of Psychiatry University Medical Center Göttingen (psychiatric patients with different diagnoses)

TABLE 1 | Demographic, clinical, and laboratory data of patient groups.

	Rural environment PAB + (*N* = 7)	Rural environment PAB- (*N* = 19)	Statistics rural PAB + VS PAB-	Urban environment PAB + (*N* = 29)	Urban environment PAB- (*N* = 110)	Statistics urban PAB + VS PAB-
Age Years	57.6 ± 13.3	66 ± 14	0.58	62.6 ± 16	54 ± 18	<0.05*
Gender (Female)	3/7 (43%)	13/19 (68%)	0.37	13/29 (45%)	58/110 (53%)	0.53
Inhabitants	2406 ± 1363	2529 ± 1761	0.09	65937 ± 50918	59386 ± 82122	0.46
Psychiatric syndromes						
Apathic	1/7 (14%)	3/19 (16%)	1	3/29 (10%)	11/116 (9.5%)	1
Depressive	4/7 (57%)	14/19 (59%)	0.64	17/29 (59%)	62/116 (53%)	0.68
Hostility	0/7 (0%)	1/19 (5%)	1	1/29 (3%)	6/106 (6%)	1
Maniforme	0/7 (0%)	0/19 (0%)	1	0/29 (0%)	1/106 (0.9%)	1
Neurologic	0/7 (0%)	3/19 (16%)	0.54	3/29 (10%)	16/106 (15%)	0.76
Obessive-Compulsive	0/7 (0%)	0/19 (0%)	1	0/29 (0%)	8/106 (7,5%)	0.20
Parahallucinatory	2/7 (29%)	6/19 (3.2%)	1	2/29 (7%)	29/106 (27%)	<0.05*
Psychorganic	6/7 (86%)	17/19 (91%)	1	21/29 (72%)	81/106 (77%)	0.63
Vegetative	1/7 (14%)	2/19 (11%)	1	0/29 (0%)	7/106 (7%)	0.34
Psychiatric diagnoses						
F00-F09	3/7 (43%)	8/19 (42%)	1	21/29 (72%)	57/110 (52%)	0.06
F10-F19	0/7 (0%)	1/19 (5%)	1	0/29 (0%)	2/110 (2%)	0.34
F20-F29	2/7 (29%)	4/19 (21%)	0.64	2/29 (7%)	19/110 (18%)	0.24
F30-39	2/7 (29%)	4/19 (21%)	0.64	4/29 (21%)	27/110 (25%)	0.31
F40-49	0/7 (0%)	0/19 (0%)	1	2/29 (7%)	2/110 (2%)	0.17
F60-69	0/7 (0%)	1/19 (5%)	1	9/29 (31%)	20/110 (18%)	0.19
Autoimmune disease	1/7 (14%)	2/19 (11%)	1	1/29 3%)	2/110 (2%)	0.51
Tumor	1/7 (14%)	7/19 (37%)	0.37	9/29 (31%)	20/110 (18%)	0.17
Neurological deficit	3/7 (43%)	8/19 (42%)	1	12/29 (42%)	52/110 (47%)	0.67
CSF						
Cell count (<5 MG/L)	1 ± 1.2	0.37 ± 0.49	0.21	1.4 ± 2.3	1.7 ± 7.7	0.53
Total protein count (MG/L)	507 ± 124	406 ± 96	0.08	704 ± 222	418 ± 205	0.76
Intrathecal igg synthesis	1/7 (14%)	0/19 (0%)	0.27	3/29 (10%)	11/103 (11%)	1
Blood brain barrier bisturbance	2/7 (29%)	1/19 (5%)	0.59	3/29 (10%)	24/103 (23%)	0.19
T tau protein (<450 PG/ML)	365.7 ± 369	311 ± 444	0.79	456 ± 320	421 ± 339	0.89
P tau 181 (<61 PG/ML)	71 ± 68	66 ± 46	0.88	82 ± 61	69 ± 36	0.19
Aß42 (>450 PG/ML)	1119 ± 552	1071 ± 473	0.80	1081 ± 624	1084 ± 603	0.78
Aß40	11378.5 ± 63333	11342 ± 3823	0.99	11597 ± 6192	11001 ± 5820	0.66
Ratio Aß42/Aß40 (X10: > 0.5)	1.15 ± 0.63	0.92 ± 0.42	0.34	1 ± 0.55	1.01 ± 0.56	0.78
MRI						
Generalized atrophy	0/5 (0%)	10/18 (55%)	< 0.05*	9/25 (36%)	30/95 (32%)	0.81

(Continued)

TABLE 1 | (Continued)

	Rural environment PAB + (N = 7)	Rural environment PAB- (N = 19)	Statistics rural PAB + VS PAB-	Urban environment PAB + (N = 29)	Urban environment PAB- (N = 110)	Statistics urban PAB + VS PAB-
Focal atrophy	3/5 (60%)	6/18 (33%)	0.34	10/25 (40%)	21/95 (22%)	0.08
Hippocampal atrophy	0/5 (0%)	1/18 (6%)	1	1/25 (4%)	5/95 (5%)	1
EEG						
Temporal focal slowing	3/5 (60%)	5/9 (55%)	1	6/17 (35%)	25/80 (31%)	0.78
Temporal epileptic potentials	0/5 (0%)	0/9 (0%)	1	1/17 (6%)	2/80 (40%)	0.44
Non-temporal focal slowing	3/5 (60%)	5/9 (55%)	1	5/17 (29%)	23/80 (29%)	1
Non-temporal epileptic potentials	0/5 (0%)	1/9 (11%)	1	0/17 (0%)	1/80 (1%)	1

*Aβ42, β-amyloid 42, Aβ40, β-amyloid 40, CSF, cerebrospinal fluid, EEG, electroencephalography, mg/L, milligram per liter, MRI, magnetic resonance imaging, P tau protein 181, phosphorylated tau protein 181, pAb +, psychiatric patients with neural autoantibodies, pAb-, psychiatric patients without neural autoantibodies, pg/ml, pikogram/milliliter, ratio Aβ42/40, ratio β-amyloid 42/β-amyloid 40, µg/L, mikrogram per liter, Statistics: *p < 0.05 Fisher?s exact test, not significant in a later performed correction for multiple testing.*

in 2017–2020 whose neural autoantibodies we had determined for differential diagnostic reasons. Their serum and/or CSF neural autoantibodies were not routinely assessed, as this was part of taking a differential diagnostic approach when we theorized a possible organic reason for psychiatric symptoms, i.e., by excluding an inflammatory or autoinflammatory central nervous system disease. It was the clinical presentation of all patients that prompted us to undertake an extensive differential diagnosis before making a diagnosis at their admission to our hospital, which would have entailed the examination of biological samples and seeking serum or CSF autoantibodies (see below for more details). The diagnoses we made clinically are in line with the ICD10 system ranging from F00–F09, F10–F19, F20–F29, F30–F39, F40–F49, to F60–F69. Our study was retrospective in nature and is characterized by a cross-sectional design in determining neural autoantibodies in conjunction with the primary residency of patients. COVID-19 infection was excluded in the investigated patients as it would have affected the profile of neural autoantibodies. The following autoantibodies in patients were determined as a standard panel in serum and/or CSF *via* Euroline immunoblots and cell-based assays [autoantibodies against intracellular autoantibodies: amphiphysin, CV2, GAD65, HuD, Ma1/Ma2, neurochondrin (NC), Ri, TR, Yo, and Zic4; autoantibodies against cell surface targets: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors 1/2 (AMPAR1/2), Aquaporin 4, contactin-associated protein 2 (CASPR2), dipeptidyl-peptidase-like 6 protein (DPPX), gamma-aminobutyric acid B1/2 receptor (GABAB1/2R), glutamic acid decarboxylase (GAD65), Leucin Rich Glioma Inactivated Protein 1 (LGI1), N-methyl-D-aspartate receptor (NMDAR)]. This standard panel of autoantibodies was determined in all the patients by assessing the most relevant neural autoantibodies against membrane-surface and intracellular antigens, although it would make sense to assess only specific autoantibodies in association with specific psychiatric diseases, i.e., anti-basal ganglia antibodies in obsessive-compulsive disorder (9) or neural cell adhesion molecule 1 antibodies in patients with schizophrenia (10) to limit costs. However, there is no evidence to date of clear types of autoantibodies that are specific to only one psychiatric condition (4). Most neural autoantibodies can coincide with several specific psychiatric diseases and are not specific to any one disease. All of our study patients lived in the German states of Lower Saxony, Thuringia, and Hessen. Their data were investigated in conjunction with the location of their primary residence. The urban and rural populations were differentiated when we were determining their neural autoantibodies. Primary residency refers to the patients' main living location while their neural autoantibodies were being assessed. Blood and urine parameters were not systematically assessed in patients. We categorized them into five different categories depending on their primary residence: one rural and four different urban environments depending on their population numbers. We considered a town population of less than 2,000 as a rural environment. In total, 2,000–5,000 inhabitants were considered a rural town, 5,000–20,000 inhabitants were classified as a small city, 20,000–100,000 as a medium-sized city, and over 100,000 inhabitants

a large city. The population numbers in the rural and urban environments were obtained from the Landesamt für Statistik Niedersachsen (11) from the published population census. In the second step, we grouped the patients into two categories by merging the aforementioned categories according to the following procedure. We categorized an environment as rural by adding the rural and rural town environmental dimensions comprising less than 5,000 inhabitants. More than 5,000 inhabitants were then classified as an urban environment (having merged small, medium, and large city conditions). Furthermore, psychopathology was assessed by relying on patient records and was measured by the AMDP system (12). We relied on the AMDP classification system to group symptoms into syndromes. Electroencephalographic (EEG), magnetic resonance imaging (MRI), and CSF analysis data were taken from our patient database. CSF data were retrieved from lumbar puncture samples taking a differential diagnostic approach. CSF parameters, such as cell count, a blood–brain barrier disturbance, intrathecal IgG synthesis, and neurodegeneration markers, such as *t*-tau, phosphorylated tau protein 181 (p-tau181), amyloid-ß 42 (Aß42), amyloid-ß 40 (Aß40) and ratio of Aß42/40, were assessed in the Neurochemistry CSF Laboratory of the Department of Neurology, University Medical Center Göttingen. Our study followed the tenets of the Declaration of Helsinki and was approved by our local ethics committee.

Statistical Approach

We used Fisher's exact test to compare the frequencies of (1) psychiatric patients with and without serum and CSF neural autoantibodies, (2) psychiatric patients with probable or definitive autoimmune-based psychiatric syndrome vs. those psychiatric patients without neural autoantibodies and (3) psychiatric patients with CSF autoantibodies and those with no autoantibodies at all. The age, number of inhabitants, and CSF parameters, such as cell count, protein content, and neurodegeneration markers, were assessed by paired Student's *t*-tests with a later performed Bonferroni correction for multiple testing. A *p*-level of $p < 0.05$ was considered as a relevant difference between groups.

RESULTS

Description of Psychiatric Patients' Cohorts

In our cohort ($n = 167$ psychiatric patients), we identified 36 patients with serum or CSF autoantibodies (pAb +). In total, 131 psychiatric patients had no autoantibodies (pAb-). These patients were not infected with COVID-19 (an exclusion criterion of the study) as mentioned in the methods section. No differences emerged between the frequency of taking certain psychopharmacologic drugs between pAb + and pAb- groups [pAb + : antidepressant drugs in 15/36 (42%), antipsychotic drugs in 7/36 (19.4%), mood-stabilizing drugs in 2/36 (5.5%), anxiolytic drugs in 1/36 (2.8%), hypnotic drugs in 1/36 (2.8%), and in 1/36 (1.5%) antidementia drugs; pAb-: antidepressant drugs in 57/131 (43.6%), antipsychotic drugs in 37/131 (28.6%), mood-stabilizing drugs in 9/131 (6.9%), mood-stabilizing drugs in 19/131(14.5%), and also anxiolytic and antidementia drugs in 2/131 (1.5%)]. According to our criteria (4), of the psychiatric patients presenting neural autoantibodies, 13/36 (36%) had a probable and 11/36 (31%) a definitive autoimmune-based psychiatric syndrome (the former and latter were defined as paAb + patients). Applying the Graus criteria (5) yielded results resembling the application of the Hansen criteria (4), as according to the Graus et al. criteria, 11/36 (31%) patients had possible autoimmune encephalitis and 12/36 (33%) definitive autoimmune encephalitis. In total 12 of 36 (33%) of the pAb + patients had CSF autoantibodies and were classified as pCSFAb + patients. **Figure 1** depicts the spectrum of neural serum and CSF autoantibodies in pAb + patients in urban and rural environments. The distribution of psychiatric syndromes in pAb + and pAb- patients is depicted in **Table 1**. The pAb + and pAb- patients in an urban environment as primary residency did not differ in the terms of patient's age, gender, number of city inhabitants, CSF data, MRI data, and EEG data (**Table 1**). Furthermore, the pAb + and pAb- patients in a rural environment as primary residency did not differ in terms of patient age, gender, CSF data, MRI data, or EEG data (**Table 1**). However, we observed (as a non-significant trend after correction for multiple testing) that pAb + patients were older than the pAb- patients living primarily in an urban environment. Moreover, we detected (as a non-significant trend after correction for multiple testing) fewer paranoid hallucinatory syndromes in pAb + compared with pAb- patients living primarily in an urban environment. The occurrence of psychiatric diagnosis according to ICD10 of pAb + and pAb- patients did not differ whether they lived primarily in a rural or urban environment (**Table 1**). Furthermore, the autoimmune diseases as conditions for autoimmunity did not differ between pAb + and pAb- patients in an urban vs. a rural setting (**Table 1**). Note that patients with and without autoantibodies were not all psychiatric patients. About 42% of pAb + and 47% of pAb- patients with a primary urban residence and 43% of pAb + and 42% pAb- patients with a primary rural residence had neurological deficits. The neurological deficits did not differ between groups living in an urban versus rural environment (**Table 1**). The frequency of tumors potentially indicating a paraneoplastic condition coinciding with neural autoantibodies does not differ between patients with and without autoantibodies living in an urban vs. rural environment (**Table 1**).

Psychiatric Patients Presenting Neural Autoantibodies in Urban and Rural Environments

The frequency of pAb + patients living in an urban environment did not differ from the frequency of pAb- patients living in an urban environment (**Figure 2A**). Furthermore, the number of pAb- patients living primarily in an urban environment did not differ from the number of pAb- patients doing so (**Figure 2B**). If the autoimmune origin is considered in particular, also paAb + patients did not differ in their frequency of living in an urban or rural environment compared with pAb- patients (**Figures 2A,B**). In addition, CSFpAb + did not differ

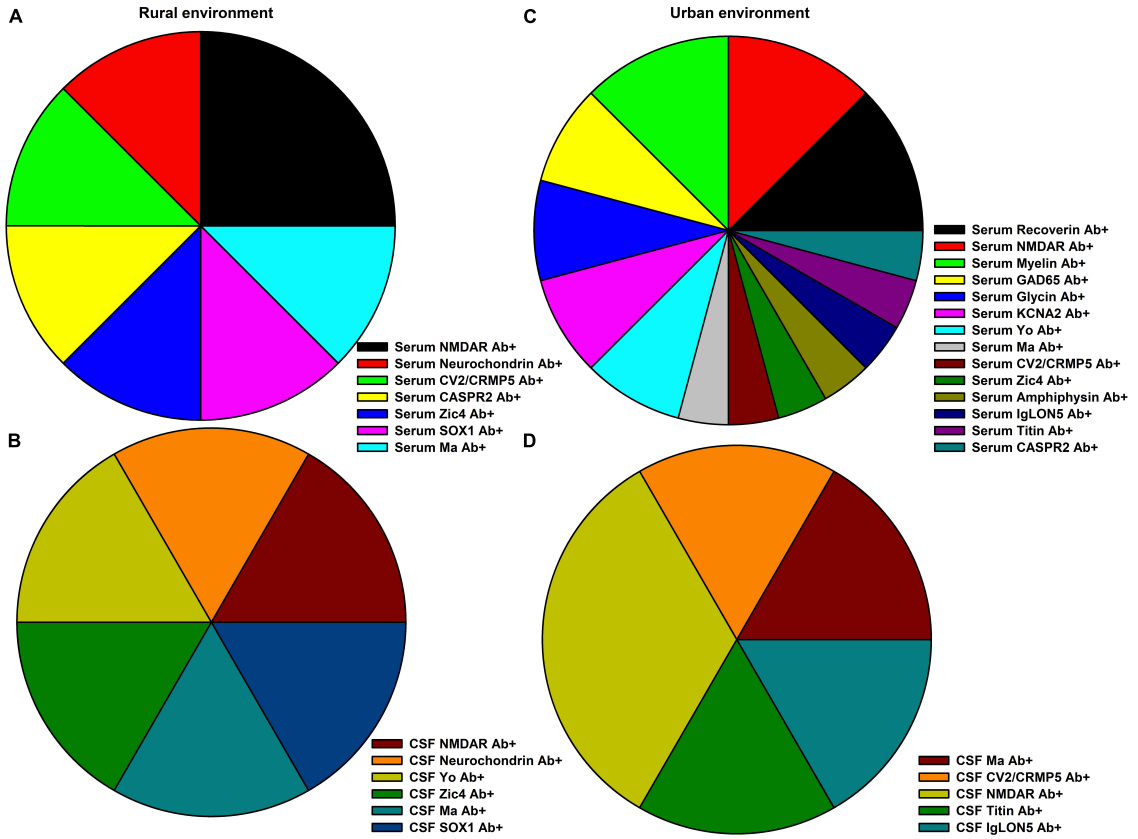

FIGURE 1 | Neural autoantibody spectrum in rural and urban environments. **(A)** The spectrum of serum and **(B)** of cerebrospinal fluid (CSF) neural autoantibody occurrence in psychiatric patients (pAb+) in a rural environment are depicted, whereas **(C)** the spectrum of serum and **(D)** of CSF neural autoantibodies in an urban environment are shown.

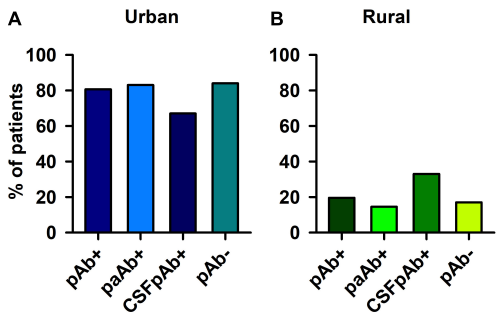

FIGURE 2 | Psychiatric patients with and without neural autoantibodies in urban and rural environment. Psychiatric patients presenting neural autoantibodies (pAb+), psychiatric patients with neural autoantibodies of a probable or definitive autoimmune origin (paAb+) and psychiatric patients with CSF neural autoantibodies (CSFpAb +) did not differ each from psychiatric patients without neural autoantibodies (pAb-) in an **(A)** urban and **(B)** rural environment.

in their frequency in urban or rural conditions from pAb- patients (**Figures 2A,B**). If the rural and urban environment situations are regarded in subdomains, no significant differences emerged between the frequency of patients living in a rural environment, rural cities, small cities, medium cities, and big cities in pAb + vs. pAb- patients (**Figure 3**). The frequency of patients living in a rural environment, rural cities, small cities, medium cities, and big cities in paAb + vs. pAb- patients did not differ (**Figure 3**). However, we noted a non-significant trend in big cities, where more pAb + (45.8%) than pAb- (26.3%) live, but this was an insignificant trend (**Figure 3**, Fisher's exact test, $p = 0.08$). Furthermore, we detected no difference in the frequency distribution when investigating only patients with pCSFAb + compared with pAb- patients (**Figure 3**). Interestingly, as with pAb + patients, we observed a potentially relevant trend, namely that the frequency of pCSFAb + patients (50%) living in big cities is higher than that of pAb- patients (31%) living in big cities (**Figure 3**, Fisher's exact test, $p = 0.20$).

DISCUSSION

Our findings indicate that autoantibody-associated psychiatric disease is not more frequent than psychiatric disease without antibodies in rural vs. urban environments. These findings do not contradict studies that detected a higher frequency of psychiatric disease in an urban environment, as the focus of this study is the frequency of neural autoantibodies in psychiatric

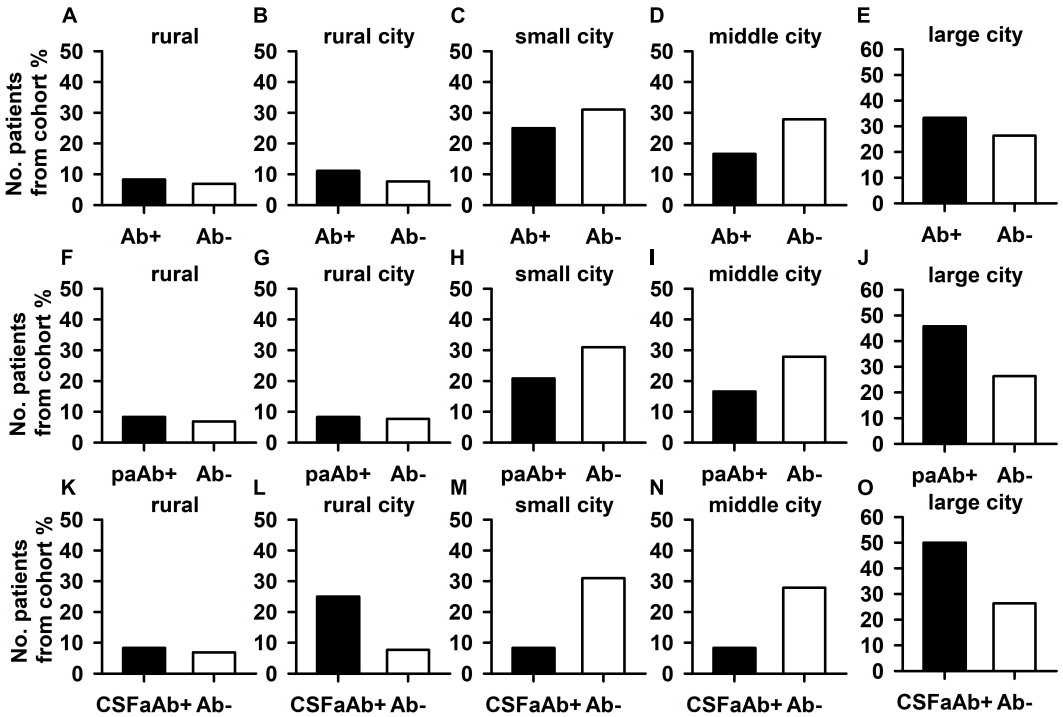

FIGURE 3 | Psychiatric patients with and without neural autoantibodies in different dimensions of an urban and rural environment. The percentages of psychiatric patients with neural autoantibodies (Ab+) did not differ from those without neural autoantibodies in all dimensions: rural (less than 2,000 inhabitants) **(A)**, rural town (2,000–5,000 inhabitants) **(B)**, small city (5,000–20,000 inhabitants) **(C)**, middle city (20,000–100,000 inhabitants as a medium-sized city), **(D)** and large city (over 100,000 inhabitants a large city) **(E)**. Furthermore, the percentage of psychiatric patients with neural autoantibodies and a probable or definitive autoimmune origin (paAb+) did not differ from the percentage of those without neural autoantibodies in all dimensions: rural **(F)**, rural town **(G)**, small city **(H)**, middle city **(I)**, and large city **(J)**. Finally, also the percentages of psychiatric patients with CSF neural autoantibodies (CSFaAb+) did not differ from those of patients without neural autoantibodies in all dimensions: rural **(K)**, rural town **(L)**, small city **(M)**, middle city **(N)**, and large city **(O)**. Ab+, neural autoantibody positive, Ab-, neural autoantibody negative.

patients, and not a psychiatric disease *per se*. Nevertheless, we identified two non-significant trends in our psychiatric patient cohort that might reveal a direction to follow in larger studies with more homogenous psychiatric patient cohorts regarding diagnosis: in a large city environment, the frequencies of neural autoantibody-associated psychiatric syndromes, and the CSF neural autoantibodies associated with the psychiatric disease are higher than they are in autoantibody-negative psychiatric patients. This trend is supported by our hypothesis that neural autoantibodies and psychiatric disease coincide more often in cities compared with psychiatric disease alone. Due to the lack of significance, our hypothesis of a higher frequency of psychiatric patients presenting neural autoantibodies compared with those without neural autoantibodies could not be confirmed.

Nevertheless, one potential explanation for the trend we observed is that viral stimuli may later affect the production of neural autoantibodies. A further explanation for the observed trend is that autoimmune diseases can be triggered by environmental conditions, such as air pollution. Air pollution can trigger increased proinflammation characterized by higher proinflammatory cytokine levels and a switch of T-cells resulting in a higher Th-17 expression, as shown in a study of the autoimmune disorder rheumatoid arthritis (13). Another possibility is that the social environment in cities might affect the development of serum autoantibodies in diabetes, which is observed more often in blue- than white-collar city regions (14). These studies provide various possible explanations for the trend we observed. More investigation is needed in large cohorts in different regions and varying social-environmental contexts measuring the incidences of diverse viruses to investigate this tendency, which is even more pronounced in psychiatric patients with an autoimmune-based psychiatric syndrome or presenting CSF neural autoantibodies. Exposure to many non-pathogenic environmental microorganisms, such as those in rural environments could have a protective effect in preventing the development of diabetes type 1, an autoimmune disease (15) as our hypothesis proposes. Furthermore, environmental factors might also have an influence on the associated cancers present in psychiatric patients with autoantibodies, namely, in 31% of those living in a rural and in 14% living in an urban environment. However, we detected no differences in the presence of cancer between patients with and without autoantibodies in a rural vs. urban environment, thus this factor can probably be weighted as a minor factor contributing to our cohort's findings. Apart from the relationship between psychiatry and autoimmunity, other aspects should be kept in mind, i.e., city living may offer

residents more protection from certain psychiatric diseases as Stier et al. recently showed regarding depressive symptoms (16). This protective effect might be also disease-specific as social-environmental activation plays a major role in specific psychiatric diseases, such as depression. Suicidality and self-harm (as other major psychiatric clinical features) are higher in cities than in the countryside in the United Kingdom and Ireland (17).

Limitations

Our autoantibody-positive patient cohort possesses enormously heterogeneous autoantibodies, all of which could have different effects. We could not examine these diverse effects as our case numbers are too low to draw relevant conclusions. Another study limitation to mention concerns the relevant age difference as a tendency in patient groups with and without neural autoantibodies living in cities as their primary residence. More large-scale studies are therefore necessary to investigate any systematic age effect that might affect our findings. Surprisingly, we have also detected a higher proportion of patients with a paranoid hallucinatory syndrome in the group of psychiatric patients without neural autoantibodies as a tendency, a finding that contradicts previous reports on autoantibody-mediated psychosis in patients (18–21) and animal models (10) and that might depend on cohort size; this result should be replicated in larger cohorts. Another limitation is that we did not systematically screen for any head injuries, none of the patients' clinical data suggested any trauma. Another caveat is that we also did not search for autoantibodies of systemic autoimmune diseases, such as anti-dsDNA (double-stranded desoxyribonucleic acid), anti-Sm [protein complexed to six species of nuclear U1 ribonucleic acid (RNA)], anti-RNP (protein complexed to U1 RNA), etc., typical antibodies for systemic lupus erythematosus or other autoantibodies related to rheumatologic autoimmune diseases. In addition, as we did not assess prior infections systematically, we cannot claim that these infections are reasons for the later manifestation of autoimmune disease. Furthermore, our psychiatric cohort does not present the neural autoantibodies associated with neurological conditions, such as autoimmune epilepsy, as we had no patients with LGI1 autoantibodies. One would have to investigate this issue in a more homogeneous cohort of psychiatric patients with a similar diagnosis. Another caveat is that we observed a relative probability of autoimmunity (based on the Graus (5) and Hansen (4) criteria) in 64% of patients, but 36% of them presented no clear signs of any pathogenicity from the autoantibodies we detected. We thus cannot rule out that the neural autoantibodies might not be pathogenic at all in those 36% of patients. However, the observed tendency for individuals living in a large city environment to present a higher relative frequency of CSF neural autoantibodies associated with psychiatric disease (thus of highly probable autoimmune genesis) than the relative frequency of autoantibody-negative psychiatric patients should not be ignored even if the proportion of patients with possibly pathogenic neural autoantibodies is disregarded. We, therefore, maintain that our results are interesting enough to be relevant for clinicians if they are confirmed in large-scale studies. Furthermore, to better evaluate neural autoantibodies associated with peripheral inflammation, it would help to determine blood C-reactive protein in a later investigation.

CONCLUSION

Whether an environment is urban or rural has no impact on the occurrence of neural autoantibodies in psychiatric patients, as those with and without autoantibodies do not differ in rural and urban environmental constellations. However, there seems to be a tendency to observe more psychiatric patients presenting neural autoantibodies and a psychiatric disorder of potential autoimmune origin in large cities than psychiatric patients who lack autoantibodies. This trend should be further investigated in large-scale trials, as there is research evidence that specific factors in cities accelerate autoimmune processes.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the corresponding author, without undue reservation.

ETHICS STATEMENT

This study involving human participants was reviewed and approved by the Ethics Committee of the University Medical Center Göttingen. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

NH wrote the manuscript. AJ and IG performed the data collection. BT did part of the laboratory testing. JW and DF revised the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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The influence of natural environments on creativity

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This study investigated the effects of different natural environments on attention restoration and creativity. To compare the restorative benefits based on the degrees of perceived naturalness in urban areas, this study categorized environments into three types of perceived naturalness and tested the effect on one's creativity. The urban campus was selected as the study site, representing high-, medium-, and low-perceived naturalness photosets downloaded from Google Street Map images as experimental stimuli. The study invited 100 subjects to take the Abbreviated Torrance Test for Adults (ATTA), which measures creative thinking by viewing the onscreen photosets of the experimental stimuli. In addition, this study asked participants to complete the Perceived Restoration Scale (PRS) questionnaires. The results showed that high- and medium-perceived naturalness in the urban-campus site was superior to low-perceived naturalness in creative performance. In addition, there were significant differences in elaboration and flexibility for different degrees of perceived naturalness. Various degrees of perceived naturalness showed a substantial correlation between PRS scores and ATTA scores. The attention restoration benefits of high- and medium-naturalness environments improve creativity. Our study indicates that viewing natural environments stimulates curiosity and fosters flexibility and imagination, highly natural environments distract our minds from work, and the benefits of attention restoration can improve the uniqueness and diversity of creative ideas. This study provides a reference for creative environmental design and supports further understanding of nature's health and creativity benefits in urban areas.

KEYWORDS

attention restoration, creative thinking, inspiration, naturalness, urban green space

Introduction

Studies in environmental psychology have found that natural environments have psychological benefits, such as attention restoration theory (ART) (1) and stress reduction theory (SRT) (2), that greatly enhance essential human health. Previous study found that the forest landscape elicits one's ability to provide more detailed answers than an urban street landscape (3). However, most studies have focused on the psychological benefits of natural environments for self-actualization rather than for creativity. Exploring the degree of naturalness in urban green spaces would help us understand the effect on creative thinking and to understand the benefits of restorativeness.

Past research has shown that natural environments, or environments with natural elements, enhance creative performance more than urban environments (4–7). Dealing with the daily work process and preparing and understanding new work problems could consume our directed attention, leading to attention fatigue. Exposure to environments with restorative characteristics (i.e., being away, fascination, extent, compatibility) compared with artificial environments can promote recovery from attention fatigue (1). In addition, opportunistic assimilation theory says that the visual environment may stimulate inspiration and encourage creative thinking (8, 9), and nature characteristics such as bio-inspired, fascination attributes enhance one's creativity ability (10, 11). In addition, human perceived naturalness affects one's visual quality of the spaces (12, 13). While little research has examined the influence of the degrees of perceived naturalness in environments on creative performance, this research investigated whether environments with different perceived naturalness could impact creative performance. Therefore, this study explored the relationship between the different environments' attention-recovery benefits and the subjects' creative performance.

The research objectives were as follows:

1. Explore whether different degrees of natural environment in urban settings influence attention recovery.
2. Explore whether different degrees of natural environment in urban settings have an impact on creative performance.

What is creativity?

Creativity refers to generating new and valuable ideas, identifying problems, and realizing ideas (11, 14, 15). To be innovative, ideas must be suitable for solving problems. Creativity is a process of generating ideas to manifest a problem-solving ability (16, 17) through complex cognitive methods of identifying questions, developing ideas, and then implementing the ideas. When individuals face work problems, one way to seek solutions is through divergent thinking (18). Divergent thinking means proposing many possible solutions to a problem and choosing the best solution, rather than seeking a single answer. Divergent thinking reflects many aspects of creativity and could be an essential indicator of knowing one's creative potential (16, 19). Guilford (18) pointed out that divergent thinking has four elements: fluency, originality, elaboration, and flexibility. Fluency is the ability to come up with many ideas and represents an individual's ability to recall past information widely and freely. Originality means combining different types of information to come up with innovative and unique ideas. Elaboration is the ability to express the details of an idea accurately and completely. Flexibility refers to multiple aspects of flexible thinking in response to the same stimuli. In addition, scholars have noted that the creative process has four stages: preparation, incubation, idea generation, and evaluation (14, 15). The incubation period occurs when a solution cannot be identified after sufficient preparation. The creator temporarily stops consciously thinking about the problem and directs their attention to other things. After a short rest, thoughts may flow freely in the subconscious without being restricted by general logic, generating new ideas more efficiently (14, 15).

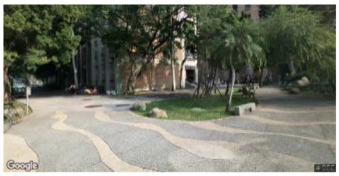
When seeking inspiration for problem-solving, the inspiration may occur as a momentary "Ah-ha!" moment or gut reaction (20). More complex problems may require more directional attention on mentally consuming thinking. Sio and Ormerod (21) believed that fatigue recovery and external stimuli could affect the incubation factors. Fatigue recovery refers to the improvement of incubation benefits after recovering from mental fatigue when the initial tasks of understanding and thinking cannot solve the problem (22). On the other hand, opportunistic assimilation theory points out that the existing resources from external stimuli (i.e., information received from the external environment) can be used as inspiration to develop ideal solutions and bring the opportunity to inspire new ideas without subjects being aware of them and with no need for attention (23).

Creativity, naturalness, and the restorative environment

Naturalness is defined as a biosphere with any type of natural element in the space. The degree of closeness to nature, such as nearness to water, plants, and other natural elements by visual perceptions, called perceived naturalness, might influence our landscape preference, restorative experience, and landscape design (12, 13, 24). In addition, information in nature stimulates ideas. In environmental design, such as landscape and architecture, biomimicry, inspired by the design method of technology transfer between biological and man-made structures in nature, is widely used in sustainable environmental design (25). Moreover, spaciousness and mystery in the natural environment elicit one's creativity performance (26).

A restorative environment provides a sense of escape from the usual, recovery from attention fatigue, and the potential to generate ideas through mind-wandering (e.g., daydreaming or freely thinking) (15). Studies point out that a natural setting with "fascination" stimulates ideas and influences creative ability, which is associated with mind-wandering (27). That is to say, natural environments easily attract involuntary attention, allowing the mind to roam freely and recover directed attention (1). The four restorative environmental characteristics bring out the conceptual statement mentioned

TABLE 1 Definitions of environmental photo content for each degree of perceived naturalness.

Group	Sample picture	Description
High naturalness (HN)		• Proximity to nature—very close to nature. • Proportion of natural elements—mainly natural elements, including flowers, trees and ground cover, with few artificial features such as trails and guardrails.
		• Environment type—campus ecological pool, farmland, or green recreational area.
		
Medium naturalness(MN)		• Proximity to nature—a moderately close-to-nature semi-artificial and semi-natural environment. • Proportion of natural elements—a balance of natural elements and artificial elements, with artificially designed streets and planting configurations.
		• Environment type—campus streets and outdoor recreation spaces.
		
Low naturalness (LN)		• Proximity to nature—very unnatural man-made environment.

(Continued)

TABLE 1 Continued

Group	Sample picture	Description
		• Proportion of natural elements—a street environment with few natural elements, dominated by man-made facilities such as cars, buildings, and driveways. • Environment type—artificial environments such as campus parking lots and roads.
		

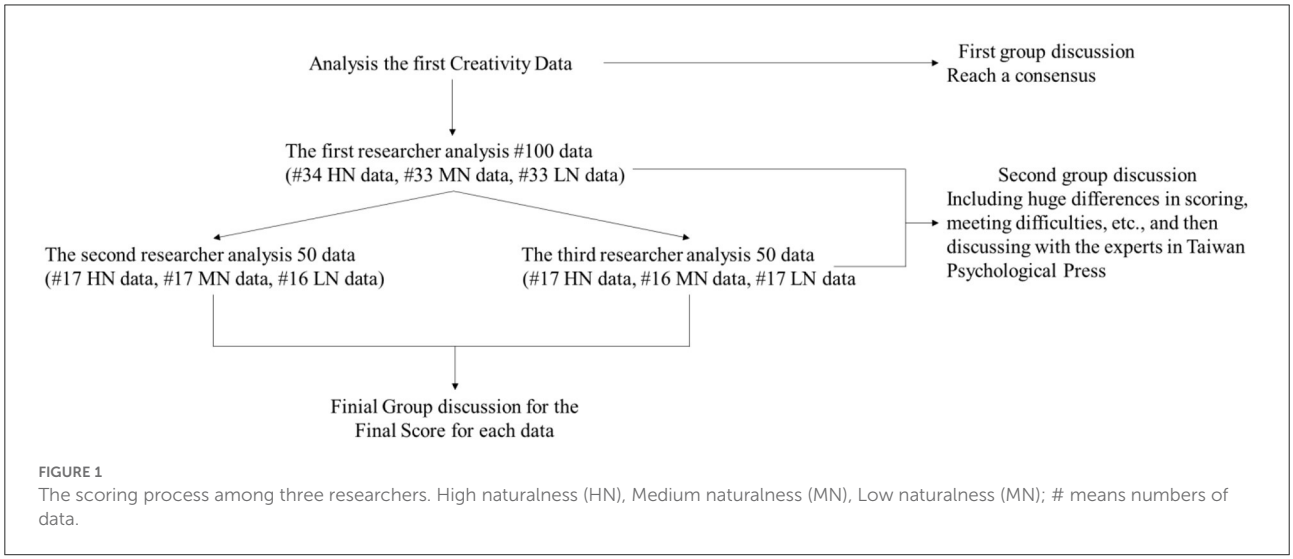


FIGURE 1
The scoring process among three researchers. High naturalness (HN), Medium naturalness (MN), Low naturalness (MN); # means numbers of data.

in ART, which includes the following. Being Away, escape from everyday life, means presenting the ego with something different from everyday life. Extent, the range of visual perceptions in a wilderness environment, is vast, and such rich, diverse environmental information provides opportunities for visual exploration in comfortable, easy-to-read ways. In addition, the concept of extent includes connectedness and scope, which gives a sense of being whole (1). Nature is rich in fascinating elements that provide opportunities for "soft" Fascination, such as waterfalls, clouds, sunsets, snow scenes, or leaves fluttering in a breeze. The intriguing qualities of the natural environment can both attract involuntary attention and restore attention. Compatibility refers to the degree to which an individual's needs and tendencies are compatible with environmental conditions.

The most important influence of the natural environment on creativity is at the creative idea stage (i.e., in the incubation period), including getting inspiration and problem-solving (7, 11). Nature beneficially enhances creativity, new ideas, and flexible thinking, while improving our attention to analyze further and develop ideas (1, 3, 7, 11). During a creative incubation period, nature walks foster calmness and spiritual rejuvenation, providing opportunities to rest and review problematic issues in a new light (11). Numerous studies have discussed the relationship between creativity and natural environments, including actual nature experience (4, 28), indoor plants, natural window views or natural environmental images (3, 6, 8, 26, 29), natural environments experienced through immersive virtual devices (30), and even quick design practice in an actual outdoor natural environment (7). All the above studies found that creativity improves in natural settings or the presence of natural elements. Since creativity relies on the benefits that individuals obtain from environmental perceptions, the degree of perceived naturalness in this study mainly refers

to the proportion of natural elements in the visual environment and how close to nature individuals judge the environment to be.

Based on these statements, this study aimed to explore the effects of different degrees of perceived naturalness in the urban environment on attention restoration and creativity. First, does the proportion of natural elements in an image affect attention restoration? Second, is creative performance affected by perceived environmental naturalness?

Materials and methods

The Research Ethics Committee of the National Taiwan University approved this study (approval number: 202103HS033). The campus of National Taiwan University, which was selected as the research site, could be regarded as a small prototype of urban greenery. Using the ArcGIS software's fishnet tool, we set sampling points every 60 meters (about half a minute's walking distance) in the research area. We collected the latitude and longitude coordinates of 498 sampling points. Google Street Map images were downloaded for each sampling point to build a database of environmental photos. Operational photo parameters include viewing angle parallel to the line of sight, uniform, and the photo size (200 pixels by 200 pixels in download by the free version). After excluding 13 sampling points with no associated photos, a total of 485 street-view environmental photos remained. Next, reviewing these photos and eliminating those with unacceptable compositions (such as dark, distorted, or blurred images that might affect visual perception or photos with excessive repetition of similar scenery), 141 photos remained.

Selected different degrees of perceived naturalness

We used the definition of perceived naturalness within the criteria shown in Table 1. We then divided the research stimuli into high-, medium-, and low-perceived naturalness in urban environments. The researchers selected 20 representative environmental photos for each group (i.e., 60 photos) from the 141 remaining photos. Five professional landscape architecture researchers were invited to evaluate the photos to verify them, with an inter-rater reliability statistic of 0.88 ($p < 0.001$). The evaluations of perceived naturalness were based on the statement, "I think the environment of this place is very natural." They rated the perceived naturalness on a seven-point Likert scale (1 = strongly disagree, 7 = strongly agree). Finally, all the photos were classified as high-perceived naturalness ($M = 5.20$, $SD < 0.35$), medium-perceived naturalness ($M = 3.74$, $SD < 0.47$), and low-perceived naturalness ($M = 1.64$, $SD < 0.56$) environments in three experimental groups. There were 18 photos in each group, making a total of 54 photos (samples shown in Table 1).

Perceived restoration scale

As reviewing numerous studies, studies did not specifically mention the order effect as discussing the restorativeness in different environments (31–34), so as in the short version of PRS developed by Berto (35). Based on the ART and the relationship between the natural environment and creativity ability, this study used the short version of the PRS developed by Berto (35) to measure restorative characteristics in different degrees of perceived naturalness in the urban settings. In addition, our study used the same order to test what subjects feel restorativeness in different naturalness urban.

Using this version, we translated the original text by researchers and discussed with native speakers the meaning of sentences accurately. Five items represented the distance from daily life and attractiveness in the environment: being away, fascination, coherence, scope, and compatibility. In ART, extent refers to a sense of coherence to the place and feeling a sense of scope in exploring the settings (1). Therefore, this study used the concepts of coherence and scope to measure restorativeness. Each item was scored on a five-point Likert scale (1 = strongly disagree, 5 = strongly agree). The study used average scores on each restorative characteristic and average total scores on the PRS to verify our research.

Measurement of creative performance

The abbreviated Torrance test for adults

The ATTA measures creative performance. The test generates quantitative data, normative data, and valid standardized scores (16, 36). The purpose of the test was to determine the association between divergent thinking and stimuli during the creative thinking process of subjects and to provide an index to evaluate creative performance in a specific state. The study used the version that Taiwan Psychological Press published (https://www.psy.com.tw/ec99/ushop20128/GoodsDescr.asp?category_id=119&parent_id=87&prod_id=84150), which could be tested from February 2020 to January 2022.

According to the order of the experiment in the instruction manual, it consisted of three activities—one verbal activity and followed up with two figural activities published by Taiwan Psychological Press. Consequences tasks were used in the verbal activity test by asking participants to answer the hypothetical situations presented by the questions within a time limit. This type of test is similar to that of Hass (37). In Figural Activity 1, the subjects were asked to use the fragments of geometric figures provided in the questions to finish the drawing within a given

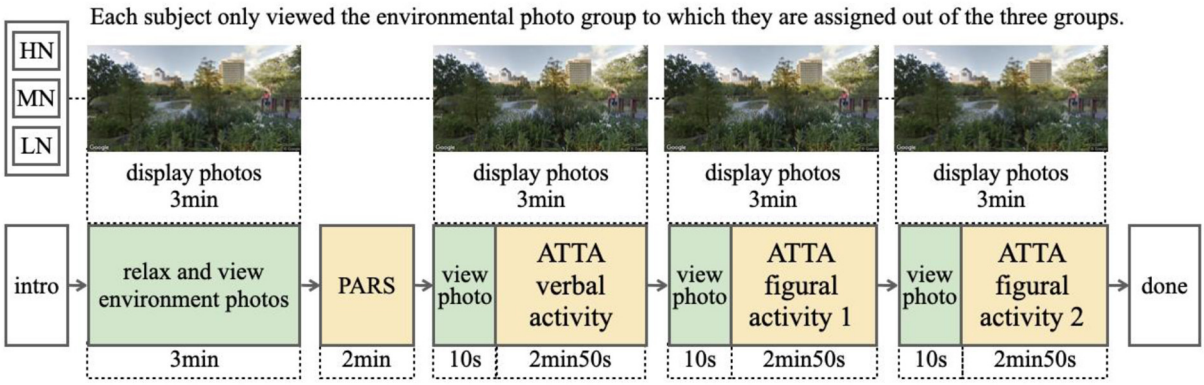


FIGURE 2
Experiment process.

TABLE 2 One-way ANOVA analysis of PRS for environments with different degrees of perceived naturalness in urban settings.

	HN ($n = 34$) M. (S.D.)	MN ($n = 33$) M. (S.D.)	LN ($n = 33$) M. (S.D.)	F	p	Post test
Being away	4.12 (0.59)	3.79 (0.82)	3.15 (0.97)	12.341	0.000	HN>LN*
						MN>LN*
Fascination	3.82 (0.76)	3.88 (0.96)	3.45 (0.87)	2.352	0.101	
Coherence	2.97 (0.97)	3.52 (0.83)	3.52 (0.76)	4.517	0.013	LN>HN*
						MN>HN*
Scope	3.82 (0.67)	3.97 (0.77)	3.12 (0.89)	11.111	0.000	HN>LN*
						MN>LN*
Compatibility	3.76 (0.92)	4.15 (0.87)	3.39 (0.93)	5.725	0.004	MN>LN*
PRS	18.50 (2.29)	19.30 (2.89)	16.64 (2.98)	8.293	0.000	HN>LN*
						MN>LN*

*$p < 0.05$.

time frame. In Figural Activity 2, the subjects were asked to use the nine identical graphics on the test paper to draw pictures while naming each sketch they drew.

Scoring of ATTA

The creativity evaluation method used Guilford's (18) four divergent thinking concepts for evaluation scoring criteria—fluency, originality, elaboration, and flexibility. In scoring fluency, people who come up with many ideas or solutions have the fluency ability of creativity. We used the number of those ideas as the scoring standard without incorrect answers. The original score in fluency is one and up to twenty-two. Originality stands for creating unusual, new, and unique ideas. The original score in originality is zero and up to seven. The elaboration scored as what participants presented the details, but not just the core idea. The original score in elaboration is zero and up to thirteen. Flexible thinking means creating more satisfactory answers as reposing to the same situation. Therefore, the original score in flexible is zero up to six. Those four indicators of creativity were scored as "original scores" based on the Torrance Creativity Test Instruction Manual (36). After scoring the four original scores, the scores were converted to a "nine-point normalized score", from eleven to nineteen, conducive to comparison and discussion of the four indicators. The total normalized score (A) of the four indicators, represented creative performance.

In addition, the statistical analysis of the original scores of each activity and the total normalized score of creativity were then tested for the effect of different perceived naturalness. Another scoring system to verify one's details on creativity is called the "standard reference scores (B)" for 0, 1, and 2 points within each of the 15 indexes, such as the abilities of imagination, novelty, abstraction, feelings, stories, or fantasy and then added those points together.

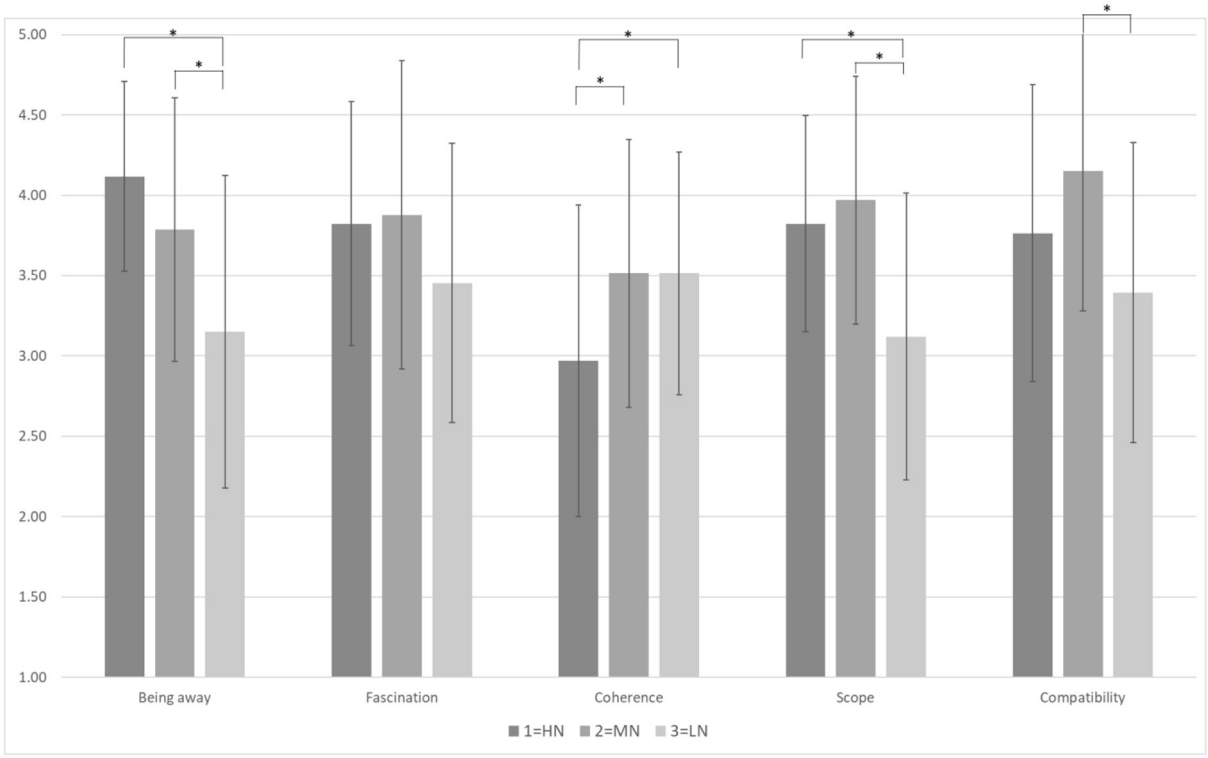


FIGURE 3
The effect of different degrees of perceived naturalness on restorativeness. *N = 100, HN (n = 34), MN (n = 33), LN (n = 33), *p < 0.05. This figure shows the five indicators of restorative of their means scores in different degrees of perceived naturalness. The error bars indicate the standard deviation.*

TABLE 3 One-way ANOVA analysis on the original score of ATTA's Figural Activity 2 in landscape environments with different perceived naturalness.

	HN ($n = 32$) M. (S.D.)	MN ($n = 33$) M. (S.D.)	LN ($n = 33$) M. (S.D.)	F	p	Post test
Fluency	6.06 (2.18)	6.24 (1.94)	5.76 (2.73)	0.372	0.690	
Originality	1.19 (1.18)	1.33 (1.27)	0.67 (0.92)	3.162	0.047	MN>LN*
Elaboration	3.47 (1.74)	3.00 (1.58)	1.88 (1.29)	9.099	0.000	HN>LN*
						MN>LN*
Flexibility	3.44 (1.24)	3.39 (1.25)	2.48 (1.30)	5.932	0.004	HN>LN*
						MN>LN*

*$p < 0.05$.

Finally, the Creativity Index (CI) score is an overall concept of creativity, which distinguish the different level of creativity. In addition, the CI refers to the holistic ability to analyze one's creativity in performance. It was calculated by the total normalized score (A) and the standard reference score (B). The CI score from one to seventy-six or more.

Further, three researchers were trained in the scoring method of the creativity test based on the instruction manual. In addition, the researchers had backgrounds in professional landscape environments and served as scorers. One researcher scored 100 test sheets and then invited two researchers to separately score in the second round. After that, the three researchers had a group discussion if there was a difference between the two researchers. In the meantime, researchers also included experts from Taiwan Psychological Press to discuss. After all this, the researchers reached a consensus and came up with the final score (Figure 1). Finally, after scoring all the data, they were sorted and entered statistical analysis software (Statistical Product and Service Solutions; SPSS) for subsequent analysis and discussion.

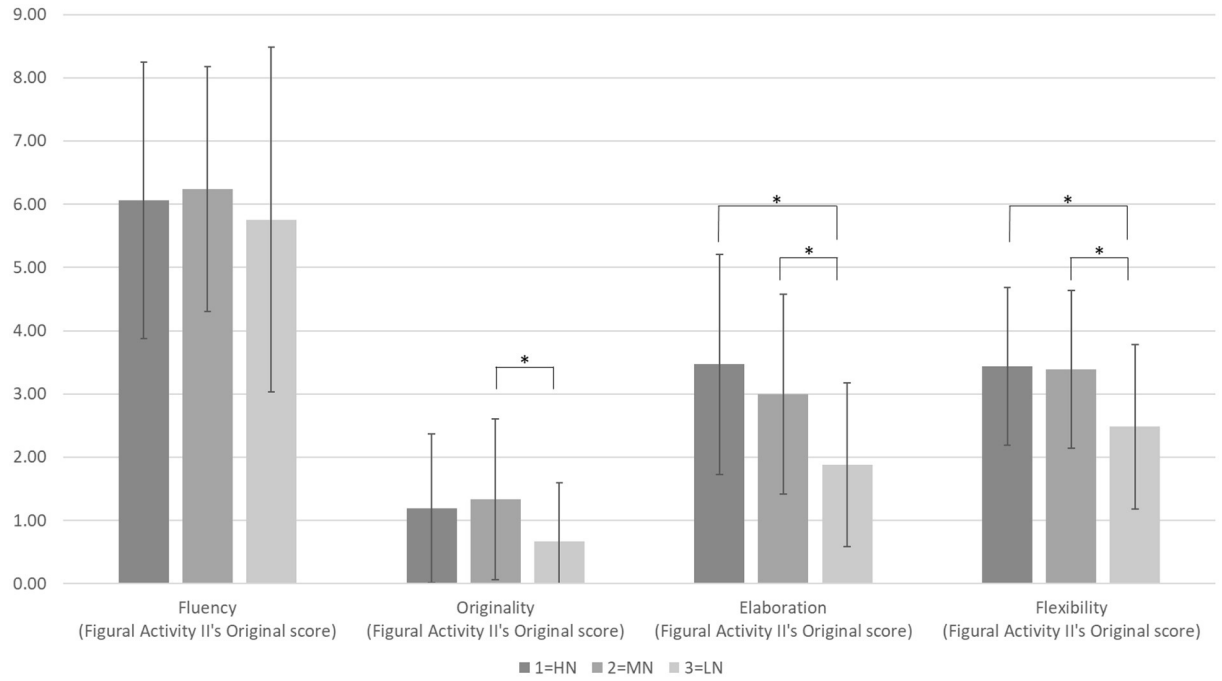


FIGURE 4
The effect of different degrees of perceived naturalness on creativity performance in Figural Activity 2. *N = 98, HN (n = 32), MN (n = 33), LN (n = 33), *p < 0.05. This figure shows the creativities indicators of their means scores in different degrees of perceived naturalness. The error bars indicate the standard deviation. Nineteen samples scored zero on "originality" in the low naturalness.*

Participants and procedure

One hundred subjects (male = 46; female = 54) were recruited online and divided into three experimental groups for high-, medium-, and low-perceived naturalness. Students over 20 years old were invited to participate in the study. The mean age was 23.1 years old. The subjects were randomly assigned to three experimental groups to view one of the photosets in the testing room for data collection. The experimental data collection included perceived attention restoration and creative performance. Attention restoration was measured using the PRS short-form questionnaire developed by Berto (35). Creativity was measured using the ATTA. The whole experiment process lasted about 30 min (Figure 2).

In more detail, each photo was displayed for 10 seconds, and each photoset of 18 photos was shown for 3 min (180 s). After viewing the photoset for the first time, the subjects completed the PRS. Next, the ATTA followed the second part of the experiment. In the meantime, as they participated in each creativity activity, the participants viewed the same photoset again. In addition, researchers told participants, "If you encounter any difficulties in the process, you can explore the environmental photos for inspirational clues for creative thinking."

Statistical approach

The study would like to test the effect of different degrees of perceived naturalness that influence one's creativity and restorativeness. Therefore, the study used Analysis of Variance (ANOVA) and Least Significant Difference (LSD) for the *post hoc* test to verify the research. The threshold for significance in $p < 0.05$ in our study. According to the creativity score, we used ANOVA to analysis on the "original score" and the "the overall ATTA normalized score".

Results

One hundred subjects participated in the experiment. One was excluded due to a lack of understanding of the content of the verbal activity, and two failed to answer the figural activity. Therefore, a total of 97 subjects were tested and separated to

verify the effect of different degrees of perceived naturalness in an urban influence on one's creativity, while not missing data in testing the effect on perceived naturalness and restorativeness.

The effect of different natural environments on restorativeness

Table 2 shows significant differences in perceived naturalness and restorative characteristics. The results show the restorative characteristics of the PRS and show that the subjects who viewed the environments with different degrees of perceived naturalness had significantly different scores for being away [$F_{(2,97)} = 12.34$, $p < 0.001$]. In the *post hoc* test, the HN group ($M = 4.12$, $SD = 0.59$) and the MN group ($M = 3.79$, $SD = 0.82$) were significantly higher than those in the LN group ($M = 3.15$, $SD = 0.97$). There was also a significant difference in scope [$F_{(2,97)} = 11.11$, $p < 0.001$]. The *post hoc* showed the HN group ($M = 3.82$, $SD = 0.67$) and the MN group ($M = 3.97$, $SD = 0.77$) were significantly higher than for the LN group ($M = 3.12$, $SD = 0.89$). There was a significant effect on perceived naturalness and compatibility [$F_{(2,97)} = 5.73$, $p < 0.01$]; the *post hoc* showed that the MN group ($M = 4.15$, $SD = 0.87$) was significantly higher than that of the LN group ($M = 3.39$, $SD = 0.93$). Moreover, there was a significant difference in the coherence dimension [$F_{(2,97)} = 4.52$, $p< 0.05$]. The *post hoc* results showed that the MN group ($M = 3.52$, $SD = 0.83$) and those in the LN group ($M = 3.52$, $SD = 0.76$) had significantly higher scores than the HN group ($M = 2.97$, $SD = 0.97$). Figure 3 shows each restorative effect of different perceived naturalness in urban settings. The total PRS score was significant in different natural environments [$F_{(2,97)} =8.29$, $p < 0.05$]. Through the *post hoc*, the results showed that the HN group ($M = 18.5$, $SD = 2.29$) and MN group ($M = 19.30$, $SD = 2.89$) both had a more significant restorativeness effect than those in the LN group ($M = 16.64$, $SD = 2.98$). The overall results aligned with Kaplan and Kaplan's ART (1), that is, environments with higher environmental perceived naturalness had the characteristics of recovering one's attention.

The environment for the HN group included ecological pools, farmland, and other environments dominated by natural elements, whereas the environments for the MN and LN groups contained mainly artificial features. In addition, the main campus squares, sidewalks, driveways, and other environmental features were visually arranged more neatly and were more easily identified. Finally, the average score for the fascination dimension did not reach a significant level ($p > 0.05$). According to Kaplan and Kaplan (1), fascination is a attractive element or phenomenon in nature. In our study, the street scenes used in the research photos were familiar to most students and perhaps less appealing. It could be difficult for participants to feel a sense of attraction through the selected photos.

The effect of different natural environments on creative performance

The ATTA consists of three activities. The original scores for each activity were first calculated during the scoring process, and the subjects' scores were compared with the Taiwan norm scores. We then tested the effects on different perceived naturalness. Creative thinking requires different abilities, depending on the type of activity. Therefore, the original scores used in each activity and the overall normalized score for ATTA creative performance was used to examine the effect on different naturalness.

The first activity was a verbal activity. There was no significant difference in the original scores for creativity for different degrees of perceived naturalness in the ability of fluency [($F_{(2,96)} = 1.17$, $p = 0.32$] and originality [$F_{(2,96)} = 1.68$, $p = 0.19$]. The second activity was Figural Activity 1, for which the original score showed no significant effect on fluency [$F_{(2,95)} = 1.40$, $p = 0.25$], originality [$F_{(2,95)} = 2.78$, $p = 0.76$], and elaboration [$F_{(2,95)} = 1.25$, $p = 0.29$] within different perceived naturalness. The third activity refers to Figural Activity 2. Table 3 and Figure 4 show the results of the original scores on originality [$F_{(2,95)} = 3.16$, $p < 0.05$)], elaboration [$F_{(2,95)} = 9.10$, $p < 0.001$)], and flexibility [$F_{(2,95)} = 5.93$, $p < 0.01$)] and discovered a significant effect in different perceived naturalness. The *post hoc* test showed that originality in the MN group ($M = 1.33$, $SD = 1.27$) had a significantly higher score than the LN group ($M = 0.67$, $SD = 0.92$). For elaboration, the scores for the HN group ($M = 3.47$, $SD = 1.74$) and the MN group ($M = 3.00$, SD=1.58) were significantly higher than those for the LN group (M = 1.88, SD = 1.29). For flexibility, the HN group ($M = 3.44$, $SD = 1.24$) and MN group ($M = 3.39$, $SD = 1.25$) had significantly higher scores than the LN group ($M = 2.48$, $SD = 1.30$). The fluency in this Figural Activity 2 was the only one that did not play a role among the perceived naturalness. The type of figural activity used in Studente et al. (6) study resembled Figural Activity 2 in our study. The experimental results for that study showed that the creativity score for the environment with natural elements was higher, consistent with this study's results for Figural Activity 2.

In addition, the study analyzed the effect on the overall creativity score in different degrees of perceived naturalness. Table 4 shows that there is a significant effect on the total normalized score on creativity and perceived naturalness [$F_{(2,94)} = 6.83$, $p < 0.01$)]. The *post hoc* test showed that the HN group ($M = 61.87$, $SD = 4.88$) and the MN group ($M =$

TABLE 4 One-way ANOVA analysis of the overall ATTA normalized score of creativity for environments with different degrees of perceived naturalness.

	HN ($n = 31$) M. (S.D.)	MN ($n = 33$) M. (S.D.)	LN ($n = 33$) M. (S.D.)	F	p	Post test
Fluency	15.26 (1.51)	15.39(1.35)	14.73 (1.68)	1.77	0.176	
Originality	15.00 (2.00)	15.12 (2.30)	14.00 (1.92)	2.86	0.062	
Elaboration	16.26 (1.55)	15.97 (1.70)	15.03 (1.88)	4.51	0.013	HN>LN*
						MN>LN*
Flexibility	15.35 (1.92)	15.15 (2.09)	13.79 (1.80)	6.25	0.003	HN>LN*
						MN>LN*
Total normalized score	61.87 (4.88)	61.61 (5.14)	57.76 (5.06)	6.83	0.002	HN>LN*
						MN>LN*
Creative index (CI)	67.94 (7.55)	67.33 (7.20)	62.15 (6.19)	6.73	0.002	HN>LN*
						MN>LN*

*$p < 0.05$.

61.61, SD = 5.14) had significantly higher scores than the LN group ($M = 57.76$, SD = 5.06). In addition, the effect on CI in different degrees of perceived naturalness showed significant differences [$F_{(2,94)} = 6.73$, $p < 0.01$)]. The *post hoc* test showed that the HN group ($M = 67.94$, $SD = 7.55$) and the MN group ($M = 67.33$, $SD = 7.20$) had significantly higher scores than the LN group ($M = 62.15$, $SD = 6.19$). Considering the four dimensions separately, subjects viewing environments with different degrees of perceived naturalness showed significant differences in elaboration [$F_{(2,94)} = 4.51$, $p < 0.05$)]. The results of the *post hoc* test showed that the HN ($M = 16.26$, $SD = 1.55$) and MN ($M = 15.97$, $SD = 1.7$) groups could elicit more elaboration ability in describing the activities than in the LN ($M = 15.03$, $SD = 1.88$). There was also a significant difference in flexibility [$F_{(2,94)} = 6.25$, $p < 0.01$)]. The *post hoc* test showed that the HN group ($M = 15.35$, $SD = 1.92$) and the MN group ($M = 15.15$, $SD = 2.09$) had significantly higher scores than the LN group ($M = 13.79$, $SD = 1.80$). There is no significant effect on perceived naturalness and the creativity ability of fluency [$F_{(2,94)} = 1.77$, $p = 0.176$)] and originality [$F_{(2,94)} = 2.86$, $p = 0.062$)]. Overall, subjects viewing environments with high-perceived naturalness outperformed those viewing low-perceived naturalness environments in terms of creative performance scores, consistent with previous studies (6, 7, 26, 30).

Discussion

Our study tests the effect of different perceived naturalness in urban environments on creativity and restorativeness using the ATTA and PRS scales. The results proved helpful in providing relevant suggestions and references for creative environmental design and confirming the importance of natural environments for creative performance.

The findings on creative performance and different degrees of perceived naturalness in urban settings

The overall creativity scores showed a higher degree of perceived naturalness than lower, which elicits one's creativity ability from idea generation (flexibility) and the ability to express details (elaboration). There was no difference in verbal performance between the different perceived naturalness groups. According to the results, in terms of figural activity, our study inferred that those participants were students and familiar with the research sites with few changes of visual natural elements, which could be difficult for them to create many novelty ideas fluently. The results were in line with a previous study that stated there was no significant difference in the verbal performance with or without visual planting in the same classroom (6). In addition, there was no effect on Figural Activity 1. In Figural Activity 2, our results determined that regardless of high- or medium-perceived naturalness, urban environments with natural elements boost creative expression and, in particular, increase the ability for originality, elaboration, and flexibility more than in low-perceived naturalness environments. The results indicate that Figural Activity 2, with several identical graphics, fosters a sense of familiarity and good and creates ideas more than Figural Activity I. With a better understanding of the activity, the number of creative ideas gradually increases (38).

Based on past research and related theories on viewing images beforehand (39), unconsciously noticing text hints during quiz solving (23), and scanning the surrounding environment for clues during the creative process (9), it is evident that the surrounding environment can provide useful hints for the creative process and support creative thinking. The elements, compositions, and even symbolic meanings of natural

environments provide viewers with space for free exploration and imagination, which are important for generating new ideas (40). Our findings showed that perceived naturalness does play a role in one's ability to describe details, which was consistent with a previous study's findings that forest environments contribute to an ability for sophistication (3).

The findings on creative performance and restorativeness in different degrees of perceived naturalness in urban settings

This study consistently verified that the effects of different natural environments on attention restoration differ significantly. Environments with more natural elements have better perceived attention-restoration benefits than environments without natural elements. The interesting results of our findings were as follows. Being away, coherence, and scope correlated with creative performance in different degrees of perceived naturalness. High-perceived naturalness provided a sense of being away, significantly negatively related to elaboration. On the other hand, medium-perceived naturalness offers a sense of coherence and scope, which was significantly positively correlated to flexibility. A study found that the spaciousness of the natural environment positively affects creativity (11, 26). We might infer that on the psychological level, spaciousness is related to the search for innovative ideas and enables our minds to explore freely in the environment, especially for the extension to develop ideas. Being away was also highly correlated with perceived personal inspiration, suggesting that we are more motivated to think creatively when we feel disconnected from everyday life while it might limit the ability to describe details. In addition, creative performance is particularly highly correlated with flexibility, showing that natural environments away from the familiar allow us to be psychologically free and comfortable, thereby stimulating flexibility and generating diverse ideas. Therefore, our findings pointed out that the sense of coherence and scope in medium-perceived naturalness in urban settings might foster the flexibility of the creative thinking process and come up with various ideas. However, there was no significant effect on low-perceived naturalness between restorativeness and creativity.

Limitation and future study

In this study, the urban-campus environment was used as the experimental stimulus, and the perceived naturalness of the environment was used to examine its influence on creativity. The perceived naturalness of environments has a positive impact on creativity. While there are limitations in our study. The "originality" could be hard for one to elicit "novelty" ideas through different naturalness, especially in urban green space. Therefore, it might cause affect normal distribution. Future research could test the different landscape types to find out the which kinds of landscape inspire our unusual thinking. In addition, the research results can help design environments that support psychological recovery, and confer creativity benefits, serving as a reference for environmental design. Natural elements not only provide psychological recovery benefits but also enhance creative performance. However, the effect of naturalness and restorativeness on creativity or the correlation between restorativeness and creativity performance is out of our scope of this study. Future research shall think about the research topic from the perspective of cognitive psychology and also from neuroscience. Those might go deeper and find the mechanism of connecting the brain and mind to explain the psychological state and creativity performance.

Conclusion

The amount of visual natural landscape elements will affect people's perception of the perceived naturalness of the environment and thus affect the individual's creative ability and restorativeness. Past research has focused on the benefits of nature for creative performance or inspiration. As work fatigue accumulates, the number of creative ideas generated decreases (38), suggesting that restorative environmental characteristics are equally crucial for creative performance. This study indicates that viewing an environment with natural elements stimulates curiosity and a flexible imagination more than viewing an artificial environment. Also, natural environments allow our minds to temporarily detach from daily states, such as moments when we are in a daze or daydreaming, to obtain a "flash of inspiration." More unique and diverse creative ideas become possible when opinions are flexible and multiple. Studies that explored the relationship between plant diversity, flower color diversity and richness, and perceived biodiversity showed that greater flower colors and diversity could attract visible species richness, lead to a more positive aesthetic experience, provide restoration benefits (41), and affect human health (42).Therefore, improving the perceived naturalness of urban landscapes by, for example, planting flowers might confer not only psychological benefits (43) but also enhance the natural elements and elicit creative thinking. Moreover, creating a "being away" and "scope" of restorative characteristics in urban settings could inspire one's creativity. Future research could analyze the types of natural elements, such as flowers, trees, rocks, and water, to verify how natural elements affect one's performance in creativity. With the increasing demand for creativity in future competitive environments, we look forward to creating healthier and more effective lifestyles through landscape environmental design.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Research Ethics Committee of National Taiwan University (approval number: 202103HS033). The patients/participants provided their written informed consent to participate in this study.

Author contributions

C-WY: conceptualization, methodology, formal analysis, investigation, validation, data curation, and writing-original draft. S-HH: conceptualization, validation, and writing-original draft. C-YC: conceptualization, validation, supervision, project administration, and funding acquisition. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2022.895213/full#supplementary-material

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Perceived epilepsy-related stigma is linked to the socioeconomic status of the residence

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Purpose: Epilepsy is one of the most common neurological disorders with high costs for the healthcare systems and great suffering for patients. Beyond seizures, psychosocial comorbidities can have detrimental effects on the well-being of people with epilepsy. One source of social stress and reduced quality of life is epilepsy-related stigma that often occurs, e.g., due to public misconceptions or myths. Stigma has individual biological, psychological and social correlates. Moreover, environmental factors like living in remote areas are associated with stigma. However, little is known about the link between the social structure of the residence and stigma in epilepsy. Thus, we investigated the association between the structural socioeconomic status (SES) and perceived stigma in an urban epilepsy population.

Methods: This prospective, cross-sectional study examined 226 adult in-patients with epilepsy from Berlin. Multiple regression analyses were performed to check the relationship between structural SES and stigma controlling for individual-level demographic, clinical, psychological and social factors. Continuous social indices (SI) of the districts and neighborhoods ("SI district" and "SI neighborhood") of Berlin were used to measure different levels of structural SES. Non-linear relationships are tested by grouping the SI in quartiles.

Results: Both indicators of structural SES were independently linked to stigma ($p = 0.002$). For "SI district", we identified a non-linear relationship with patients from the most deprived quartile feeling less stigmatized compared to those in the second ($p < 0.001$) or least deprived quartile ($p = 0.009$). Furthermore, more restrictions of daily life ($p < 0.001$), unfavorable income ($p = 0.009$) and seizure freedom in the past 6 months ($p = 0.05$) were related to increased stigma. A lower "SI neighborhood" was associated with higher stigma ($p = 0.002$).

Conclusion: Strategies to reduce epilepsy-related stigma need to consider the sociostructural living environment on different regional levels. Unfavorable relations with the immediate living environment may be directly targeted in

patient-centered interventions. Non-linear associations with the structural SES of broader regional levels should be considered in public education programs. Further research is needed to examine possible underlying mechanisms and gain insight into the generalizability of our findings to other populations.

KEYWORDS

seizures, neuropsychology, social deprivation, neurourbanism, social disadvantage, discrimination, structural socioeconomic status

Introduction

Epilepsy is one of the most common neurological disorders and characterized by the predisposition for the (repeated) occurrence of epileptic seizures (1). Up to 7 per 1,000 people suffer from epilepsy, and in developing countries prevalence rates are estimated even higher (2). Epilepsy possesses a large burden on the individual patients, on the communities they are living in, and on their healthcare systems (3).

Stigma refers to the "co-occurrence of labeling, stereotyping, separation, status loss, and discrimination in a context in which power is exercised" (p. 813) (4) and represents a fundamental cause of health inequalities. Furthermore, stigma has large ecological costs due to its negative impact on employment, income, public views about resource allocation, and healthcare costs (5). It is a frequent concern of patients with mental, somatic, and neurological disorders and their caregivers (6). Especially people with epilepsy (PWE) may be confronted with a particularly severe stigma, as the chronic disorder is often accompanied by public misconceptions, myths and negative attitudes (6). Many PWE suffer from detrimental effects of stigma on their well-being, e.g., negative feelings or higher stress (7, 8). Stigma represents a major limitation of quality of life (QoL) for PWE, even beyond seizure-related factors or other psychosocial comorbidities (9). Up to 80% of PWE report feeling stigmatized (10), but research shows a great variability in stigma prevalence depending on the specific patient population. This underlines that it is necessary to understand correlates of stigma to identify risk populations, and to develop adequate intervention and prevention strategies.

Previous research highlights that various factors are associated with higher stigma in PWE, e.g., greater seizure severity, more antiseizure medications (ASM), more ASM adverse events, poorer QoL, as well as more depressive and anxiety symptoms (11, 12). Stigma is socially determined and occurs in many social situations. Thus, beyond the aforementioned clinical and psychological factors, stigma depends on various social characteristics of the individual and their communities. Research on stigma against various health conditions finds associations with different aspects of the socioeconomic status (SES). This concept can be subdivided in an individual SES, covering an individual's education, occupation and income, as well as a structural SES, including the social structure of an individual's living environment (13). Social aspects on both levels are linked to stigma: For instance, perceived weight stigma depends on income and social support (14). Cancer stigma is related to social constraints and income (15), or negative attitudes toward mental illnesses are more pronounced in socially deprived areas (16).

Compared to the general population, PWE have lower individual and structural SES: They are more often unemployed, have lower educational levels, or live more often in socially deprived areas (17, 18). Crucially, health of PWE is determined by social factors on both levels, as for instance access to epilepsy care, epilepsy knowledge, and outcomes of medial and surgical treatment are related to the SES. Stigma plays an important role in this framework (19). Regarding the individual SES, for instance, PWE with poorer financial conditions suffer from more stigma. Moreover, living in an environment of low structural SES may be a source of greater epilepsy-related stigma which is higher in rural compared to urban areas in African countries (12) or in public compared to private hospitals in the US (20). Public misconceptions and lack of epilepsy-related knowledge may be more pronounced in these regions and settings (11). Furthermore, worse access to treatment in socially deprived areas (21) may lead to greater reduction of daily abilities which in turn may increase stigma. However, quantitative investigations of associations between the structural SES and epilepsy-related stigma are still sparse. Results from Houston, US, suggest that stigma may not only differ between urban and rural areas but also according to structural SES differences within the same city (20).

Inhabitants of larger cities are exposed to particularly high levels of social stress. Possibly pathogenic stress may be caused or at least influenced by the co-occurrence of high population density and social isolation (22). In this framework, stigma is suggested to be part of a vicious circle: On the one hand, people with higher stress levels may be more vulnerable for stigmatized conditions. On the other hand, stigma may lead to more social isolation and elevated stress responses (4, 23). However, mechanisms of pathological urban stress are still not clear. They are addressed in the new field of neurourbanism that is connecting research in

neuroscience, architecture, mental health, urban planning, and sociology. Taking this interdisciplinary perspective, the identification of possible regional differences of stigma within a city may help to identify different risk and resilience factors (22). The current study aimed to contribute to the field of neurourbanism by shedding a more detailed light on stigma correlates within an urban population. Our results on links between perceived stigma and the structural SES of adult in-patients with epilepsy in Berlin may give hints to mechanisms in other health conditions as well. We hypothesized that a lower structural SES is associated with higher perceived stigma, even after controlling for demographic, clinical, psychological, and social characteristics on the individual level.

Materials and methods

Sample

Our cohort consisted of 226 adults (≥ 18 years old) with epilepsy residing in Berlin and represents a subsample of a larger prospective project on determinants of QoL in adults with seizure disorders (epilepsy, syncopes, psychogenic non-epileptic seizures). Diagnoses were made of the basis of detailed history taking by experienced epileptologists and, if necessary, by ictal long-term video EEG-recordings. The participants were in-patients at the Epilepsy-Center Berlin-Brandenburg, a large tertiary hospital treating patients from all over Berlin, between 01/2018 and 12/2021. Of the sample, 31% ($n = 69$) underwent long-term video-EEG monitoring in preparation of a possible surgical intervention to remove the seizure focus. Firstly, medical records were screened to apply the following exclusion criteria: (1) legal guardianship; (2) physical conditions impairing the ability to fill out questionnaires; (3) poor German language comprehension; (4) low cognitive or intellectual abilities. In addition to that, senior epileptologists with neuropsychiatric expertise had evaluated all patients to ensure that no severe mental illnesses such as schizophrenia, dementia, or bipolar disorders were present that may have resulted in invalid answers on the questionnaires. Furthermore, patients were contacted by trained neuropsychologists to exclude those with cognitive disturbances.

This study is approved by the Institutional Review Board of Charité–Universitätsmedizin Berlin (EA4/208/17). Patients were informed about a possible study participation at the beginning of their hospital stay. After they had given informed written consent, they filled out self-report questionnaires on different psychological, social and epilepsy-related variables via tablets. In rare cases of patients' difficulties with technical understanding, paper-pencil versions were used. Additional demographic and clinical variables were obtained from medical charts and databases.

Measurement

Stigma

Perceived epilepsy-related stigma was assessed with the subscale "stigma" of an adapted version of the German Performance, socio-demographic aspects, subjective evaluation (PESOS) questionnaire (24, 25). On six questions on five-point rating scales the participants indicated how they experience other people's reactions or feelings related to their epilepsy in the past 6 months (English translation of a sample item: "Are others withdrawing from you due to your epilepsy?," a full ad hoc translation can be retrieved from the Supplementary material). Values on the single items were added and transformed so that the final stigma score ranges between 0 (lowest level of stigma) and 100 (highest level of stigma). May et al. (24) reported a good internal consistency ($\alpha = 0.88$) in a sample of 196 adults and proofs of validity of the scale (24).

Clinical variables

"Seizure severity" was assessed using a German version of the Liverpool Seizure Severity Scale (LSSS), a questionnaire on seizure characteristics, consequences, impairment and controllability (26). For instance, patients are asked whether their seizure occur with loss of consciousness or whether they could suppress their seizures. Sum scores across 20 items were calculated with higher scores reflecting higher severity. Internal consistency ($\alpha > 0.7$) and validity were proven in previous research (27).

"ASM adverse events" were measured using a German translation of the Liverpool Adverse Events Profile (LAEP) (28). The occurrence of 19 common adverse events in physical, somatic and psychological domains (e.g., dizziness, stomach problems or attentional deficits) in the past 4 weeks is rated on four-point scales. The sum across all items was calculated (range 19–76), whereby values ≥ 45 indicate substantial ASM adverse events (29). The LAEP shows a good internal consistency ($\alpha = 0.85$) and was validated previously (30).

"Seizure frequency" was assessed with an adapted item of the PESOS (25). It originally consists of six categories ranging from "no seizures in the past 6 months" to "one seizure per day or more." For a more detailed description of our study population, we further added two categories indicating whether seizure freedom was present in the past year or for more than 2 years.

With respect to the current ASM treatment, "ASM mono- vs. polytherapy" at the beginning of the in-patient stay was considered.

Psychological variables

QoL was measured using the German version of the Patient-Weighted Quality of Life in Epilepsy Questionnaire

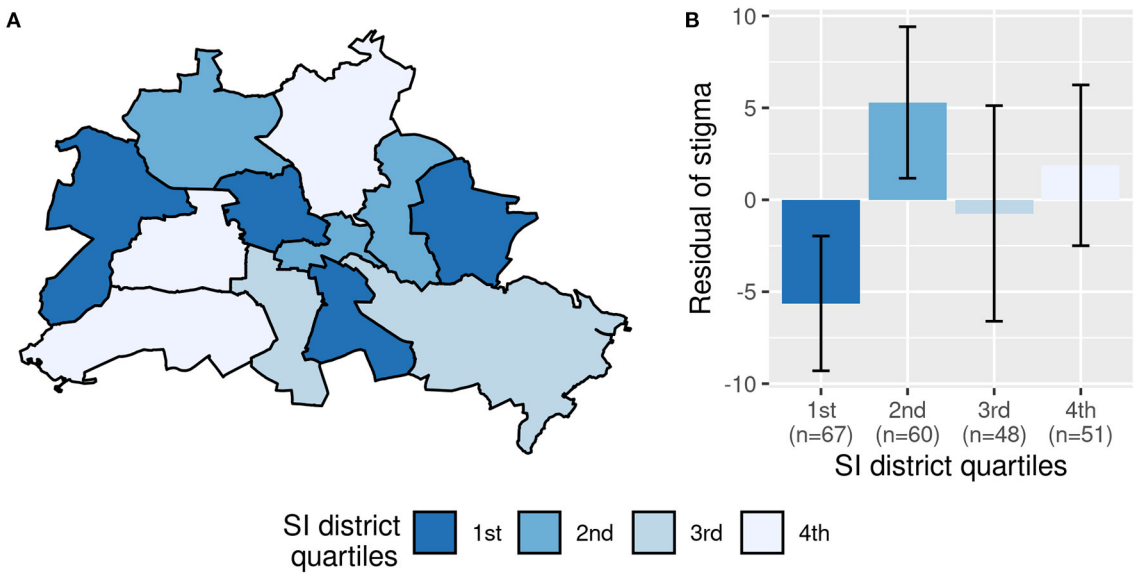

FIGURE 1
Association between perceived stigma and social index of the district ("SI district"). **(A)** shows Berlin with its 12 districts. **(B)** Displays the mean residual stigma values of the quartiles of SI district with error bars representing 95% confidence intervals around the mean. The residuals are corrected for social index of the neighborhood, restrictions of daily life, unfavorable income and seizures in the past 6 months.

(QOLIE-31-P) (31). To ensure a broad assessment of patients' QoL, we used the "Overall" subscore. It consists of two ratings about the current QoL and the QoL in the past 4 weeks. Higher scores (range 0–100) reflect better QoL. This subscale shows acceptable internal consistency ($\alpha = 0.79$) and has been validated previously (31).

A German version of the disorder-specific questionnaire Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) was used to measure "depressive symptoms" (32). This rapid screening tool contains six questions about symptoms in the past 2 weeks that do not overlap with adverse ASM events or cognitive deficits and represents a standard tool in epilepsy research (33, 34). A cut-off of $\geq$ 14 points indicates clinically significant depressive symptoms. The German version has been validated in previous studies and shows an acceptable internal consistency ($\alpha = 0.83$) (32).

"Anxiety symptoms" were assessed with the validated German version of the Generalized Anxiety Disorder 7-item (GAD-7) scale (35). This scale contains seven items on the most prominent features of generalized anxiety disorder, e.g., irritability, muscle tension, or restlessness. The scale has been validated in PWE and has a high internal consistency ($\alpha = 0.92$). Sum scores of at least 6 points indicate significant anxiety symptoms in PWE (36).

"Restrictions of daily life" were measured with the corresponding subscale of the PESOS. The scale comprises 14 items about problems with independent living, mobility, partnership, leisure time, family, friends, and mental/physical health during the past 6 months. The mean score (range 0–100) reflects the degree of perceived restrictions in daily life with high values corresponding to high disadvantage. Reliability ($\alpha = 0.91$) and validity has been proven in previous research (24).

Social variables

Structural socioeconomic status

The structural SES was measured with two differentiated social indices (SIs) of the social structure of Berlin summarizing various aspects of population, education, income, and health. These standardized scores ($M = 0$, $SD = 1$) are based on representative data of the city and are calculated for two different regional levels, 12 districts and 447 neighborhoods, by using factor analyses. Lower values for "SI district" and "SI neighborhood" indicate a lower structural SES, e.g., high unemployment rates, many inhabitants living on social welfare and low income, high premature and avoidable mortality, and many severe health problems due to tobacco abuse (37). Regional distributions are depicted in Figures 1A, 2A.

Individual social variables

Self-reports on education in the PESOS (25) were classified according to the revised International Standard Classification of Education (38). This classification system contains nine levels rating educational programs according to the degrees of complexity and specialization. Levels 0–2 were classified as "low education," levels 3–4 were classified as "medium education" and levels 5–8 were classified as "high education." The dichotomous variable

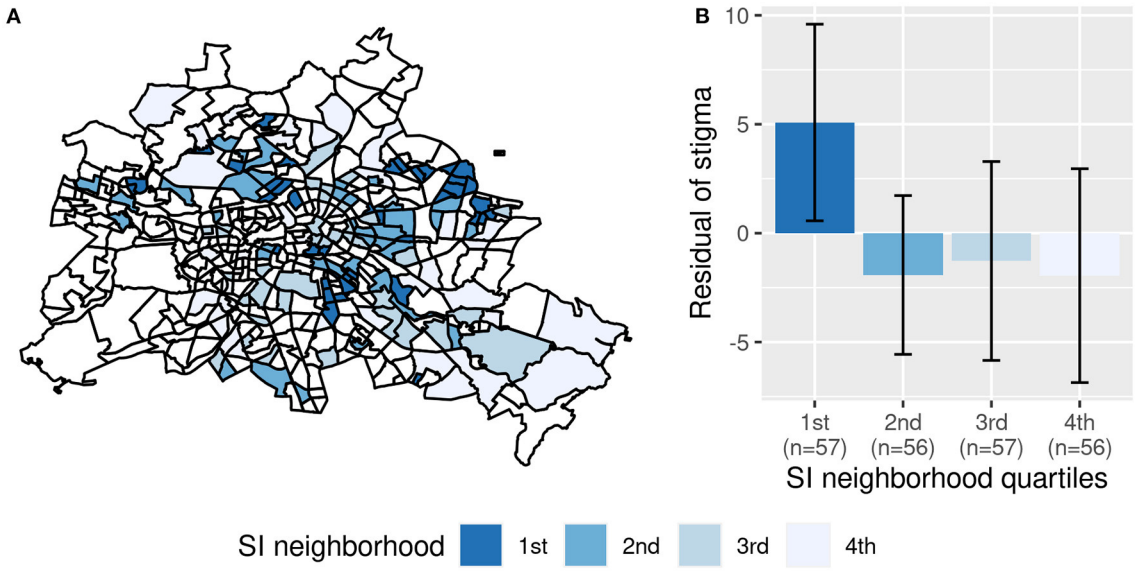

FIGURE 2
Association between perceived stigma and social index of the neighborhood ("SI neighborhood"). **(A)** Shows Berlin with its 447 neighborhoods. White areas did not contain any patients from our sample. **(B)** Displays the mean residual stigma values of the quartiles of SI neighborhood with error bars representing 95% confidence intervals around the mean. The residuals are corrected for social index of the district, restrictions of daily life, unfavorable income and seizures in the past 6 months.

on income indicated whether patients had an "unfavorable income," i.e., if they received social welfare or reduced earning capacity.

Statistical analysis

Data was analyzed with R Version 4.2.1 (39). Complete data on the relevant variables was available for all patients included in the study. We applied a multiple linear regression analysis to assess independent associations between the structural SES ("SI district," "SI neighborhood") and stigma. As possible confounders, variables identified as important correlates of stigma in the meta-analysis of Shi et al. (12) were considered. These comprise "unfavorable income," "seizure severity," "seizure frequency," "number of ASM", "ASM adverse events," "depressive symptoms," "anxiety symptoms," and "quality of life." "Seizure frequency" was initially measured using eight possible categories. For our analysis, we dichotomized the variable ("seizures in the past 6 months", "no seizures in the past 6 months)" because including all eight categories would have resulted in small sample sizes for the distinct categories. Moreover, previous research shows that patient-related outcomes are not linearly associated with seizure frequency (40). Thus, by dividing the variable in two categories according to seizure freedom allows for a better theoretical interpretation than somewhat arbitrary cut-offs of the variable with respect to other categories.

In previous studies on German patient populations, stigma was associated with restrictions of everyday life (24). This variable was not considered in the meta-analysis that served as basis for the selection of additional predictors for stigma in our study (12). However, social support, a similar related construct, was identified as important correlate of stigma, and in a German publication that was not included in the meta-analysis, "restrictions of daily life" were strongly associated with stigma (11, 24, 25). We found a comparable spearman's rho correlation between "restrictions of daily life" and "stigma" ($r = 0.59$, $p < 0.001$). Therefore, we entered this variable in the multiple regression analysis. Stigma levels did not differ between patients undergoing presurgical assessment and other patients, $t_{(224)} = -0.36$, $p = 0.72$. Relevant predictors of stigma in the multiple regression analysis were selected based on the Akaike Information Criterion (AIC) with a forward-backward selection procedure using the function "stepAIC" (41). Multicollinearity was checked using variance inflation factors (VIFs) which were all in an appropriate range (VIF < 10). Regression assumptions were checked graphically. According to the QQ-plot, normality of the residuals was violated in the first model. Therefore, influential data points according to Dffits-values were excluded and variable selection was again performed without these influential data points. The resulting model included the same predictors as the first model with similar p-values and slightly differing parameter estimates. Thus, this sensitivity analysis shows that the independent variables in the final model do not depend on extreme observations and

can, therefore, be interpreted as important predictors of stigma. As a post hoc analysis, we checked non-linear relationships using quartiles of "SI district" and "SI neighborhood." The analyses were reran with the confounders identified in the first multiple regression analysis. Differences between the quartiles were checked for statistical significance using a Bonferroni-corrected α-level of 0.008 for "SI district" and "SI neighborhood" separately. The models were compared using the AIC. Effect sizes were evaluated according to Cohen (42).

Results

Sample description

Demographic, clinical and social characteristics of the 226 patients are displayed in Table 1. In Table 2, answers on self-report questionnaires are presented. Compared to the general population of Berlin, our sample lived more frequently in socially deprived neighborhoods, $t_{(225)} = -4.13$, $p < 0.001$. For regional distributions, see Figures 1A, 2A.

Associations between stigma and the structural SES

In the univariate analysis, perceived stigma was associated with "SI neighborhood" ($r = -0.15$, $p = 0.02$) but not with "SI district" ($r = 0.04$, $p = 0.52$). The multiple regression analysis revealed that perceived stigma was independently associated with both indicators of structural SES, i.e., "SI district" and "SI neighborhood." They explained a significant independent proportion of 1.8% of the variance of perceived stigma, corresponding to a weak to small effect, $f^2 = 0.03$, 90%-CI [0.00, 0.07]. Furthermore, more restrictions of daily life, unfavorable income, and seizure freedom in the past 6 months were linked to higher perceived stigma (see Figure 3; Table 3, Model 1).

Grouping both "SI district" and "SI neighborhood" into quartiles increased model fit, AIC = 1,284 vs. AIC = 1,290 of the continuous model, suggesting a non-linear relationship with at least one of the indicators. Together, the grouped variables of "SI district" and "SI neighborhood" explained a significant independent proportion of 5.6% of the variance in perceived stigma, corresponding to a small to medium effect, $f^2 = 0.10$, 90%-CI [0.02,0.16]. Bonferroni-corrected post-hoc comparisons showed that perceived stigma was significantly higher in the most deprived neighborhood quartile compared to the least deprived neighborhood quartile (Figure 1B). Regarding the districts, perceived stigma was lower in the most deprived quartile compared to the second and fourth quartiles (see Table 3, Model 2; Figure 2B).

TABLE 1 Sample description.

Variable (*n* if not otherwise specified)	Value
Age M ± SD, years	40.48 ± 15.49
Sex female	105 (46%)
Marital status ($n = 224$)	
single	140 (62%)
married	61 (27%)
other	23 (10%)
Unfavorable income: yes	74 (33%)
Employment	
employed	106 (47%)
in education	29 (13%)
unemployed	91 (40%)
Education	
low	37 (16%)
medium	110 (49%)
high	79 (35%)
Social index of district M ± SD	0.05 ± 0.89
Social index of neighborhood M ± SD	−0.25 ± 0.90
Age of epilepsy onset M ± SD, years	23.43 ± 17.10
Duration of epilepsy M ± SD, years	17.05 ± 14.54
Type of epilepsy	
focal	187 (82.7%)
generalized	23 (10.2%)
focal-generalized	1 (0.4%)
unclassified	15 (6.6%)
Possible epileptogenic lesions in MRI: yes	97 (43%)
Additional psychogenic non-epileptic seizures present: yes	12 (5%)
Additional syncopes present: yes	4 (2%)
Number of ASM M ± SD	1.47 ± 0.93
ASM polytherapy: yes	97 (43%)
Seizure frequency	
seizure free for 1 year to 2 years	13 (6%)
seizure free for 6 months to 1 year	8 (4%)
seizure free for the past 6 months	17 (8%)
1–2 seizures in the past 6 months	43 (19%)
3–5 seizures in the past 6 months	38 (17%)
1–2 seizures per month	49 (22%)
less than 1 seizure per day but at least 1 seizure per week	34 (15%)
at least 1 seizure per day	24 (11%)

ASM, antiseizure medications; MRI, magnet resonance imaging; SD, standard deviation. Diagnoses of epilepsy, psychogenic non-epileptic seizures, and syncopes were made of the basis of detailed history taking by experienced epileptologists and, if necessary, by ictal long-term video EEG-recordings.

Discussion

This study investigated the relationship between perceived stigma and the socioeconomic status of the residence (structural

TABLE 2 Answers on self-report questionnaires.

Variable	M ± SD	Association with stigma
Perceived stigma (PESOS)	24.69 ± 21.71	
Quality of Life (QOLIE-31-P)	58.38 ± 18.19	$r = -0.39$, $p < 0.001$**
Depressive symptoms (NDDI-E)	12.87 ± 3.97	$r = 0.40$, $p < 0.001$**
Anxiety symptoms (GAD-7)	8.00 ± 4.72	$r = 0.42$, $p < 0.001$**
Restrictions of daily life (PESOS)	32.43 ± 21.47	$r = 0.59$, $p < 0.001$**
Seizure severity (LSSS)	49.29 ± 8.49	$r = 0.25$, $p = 0.001$*
ASM adverse events (LAEP)	42.00 ± 10.74	$r = 0.42$, $p < 0.001$**

ASM, antiseizure medications; GAD-7, Generalized Anxiety Disorder Screener; LAEP, Liverpool Adverse Events Profile; LSSS, Liverpool Seizure Severity Scale; NDDI-E, Neurological Disorders Depression Inventory for Epilepsy; PESOS, Performance, socio-demographic aspects, subjective evaluation questionnaire; QOLIE-31-P, Quality of Life in Epilepsy Questionnaire.
*p < 0.01; **p < 0.001.

FIGURE 3
Variables independently associated with perceived stigma in the multiple regression analysis. Presented are regression coefficients and the 95% confidence intervals of the model with continuous values of SI neighborhood and SI district (Model 1). Coefficients are standardized for the continuous predictors. SI, social index.

TABLE 3 Results of the multiple regression analysis.

	Model 1 SI continuous	Model 2 SI categorized
(Intercept)	25.8 (3.0, $p < 0.001$)	27.8 (3.7, $p < 0.001$)
SI neighborhood	−3.81 (1.54, p = 0.014)*	
SI district	2.86 (1.54, $p = 0.064$)	
SI neighborhood		
1st vs. 2nd quartile		−8.3 (3.3, $p = 0.012$)
1st vs. 3rd quartile		−9.3 (3.7, $p = 0.011$)
1st vs. 4th quartile		−10.4 (3.8, $p = 0.007$)**
2nd vs. 3rd quartile		−1.0 (3.3, $p = 0.761$)
2nd vs. 4th quartile		−2.1 (3.5, $p = 0.551$)
3rd vs. 4th quartile		−1.0 (3.2, $p = 0.743$)
SI district		
1st vs. 2nd quartile		11.9 (3.1, $p < 0.001$)***
1st vs. 3rd quartile		6.9 (3.6, $p = 0.058$)
1st vs. 4th quartile		9.9 (3.7, $p = 0.009$)**
2nd vs. 3rd quartile		−5.0 (3.5, $p = 0.153$)
2nd vs. 4th quartile		−2.0 (3.6, $p = 0.579$)
3rd vs. 4th quartile		3.0 (3.4, $p = 0.378$)
Unfavorable income	6.4 (2.6, $p = 0.015$)*	6.8 (2.6, $p = 0.009$)**
Seizures in the past 6 months	−5.3 (3.2, $p = 0.099$)	−6.2 (3.1, $p = 0.048$)*
Restrictions of daily life	0.6 (0.06, $p < 0.001$)***	0.6 (0.06, $p < 0.001$)***
R^2 / R^2 adjusted	38.9% / 37.5%	42.8% / 40.37%
AIC	1290.77	1284.12
f^2 [90%-CI interval]	0.64 [0.43;0.84]	0.75 [0.50;0.95]

Presented are unstandardized regression coefficients with standard errors and p-values in brackets. The intercept of Model 2 is calculated for the 1st quartiles of SI district and SI neighborhood as reference categories. The column contains all possible group comparisons for the quartiles. They were checked for statistical significance with a Bonferroni-corrected α-level of 0.008 and marked in the table accordingly. AIC, Akaike Information Criterion; SI, social index; *p < 0.05; **p < 0.01; ***p < 0.001. CI, confidence interval.

SES) in a sample of adult in-patients of a tertiary epilepsy center in Berlin. We found that even within one city, the structural SES on two different regional levels, i.e., immediate neighborhoods and more proximal districts, was associated with perceived stigma beyond individual-level demographic, clinical psychological, and social characteristics. Firstly, we investigated continuous measures of the structural SES, but, interestingly, our analyses showed that a categorization of the measures improved model fit. This finding indicates that the relationships between perceived stigma and structural SES follow non-linear trends. Thus, a conclusion "the higher the structural SES, the lower the stigma" is fairly too simple.

Correlates of perceived stigma

Structural SES of the neighborhood

As expected, a lower structural SES of the neighborhood was associated with higher perceived stigma. Also after categorization, living in the most deprived neighborhood quartiles was linked to the highest levels of perceived stigma. This finding extends previous research in PWE showing that perceived stigma was higher in public compared to private hospitals in the US (20). Our indicator of structural SES not only

covered the areas' healthcare systems but also includes broader indicators of population, income and health (37). Thus, one may conclude that higher social resources of different domains in the immediate living environment may be protective against stigma.

Structural SES of the district

Relationships differed for the broader regional SES level. In our continuous analyses, lower structural SES of the district was linked to lower stigma levels, which was contrary to our expectations. A closer examination of possible non-linear trends, the categorization in quartiles revealed that especially patients from the lowest SES districts reported fewer stigma than those from the second or least deprived districts. In PWE similar findings have not been identified previously. However, in women with human immunodeficiency viruses (HIV), living in areas with lower median income or more racial diversity was linked to lower perceived stigma (43). The authors concluded that a more diverse community may be protective against stigma. "SI district," our measure of structural SES, does not include indicators of diversity. However, in districts of the lowest SI quartile, e.g. Berlin-Mitte or Neukölln, the rates of people with migrant background (55 or 49% in 2021) were highest. Moreover, the diversity of the countries of origins was largest, indicating greater cultural variety in these districts (44). Epilepsy-related stigma seems to be highly culture-specific (45). Our findings may suggest that living in areas with different cultures may bring different attitudes on epilepsy closer together, which may foster understanding and tolerance, and, therefore, result in lower stigma.

Moreover, previous studies found that mental health stigma was higher in individuals of higher SES (46). As an explanation of this finding, it was proposed that people with high SES experience more controllability in their life and more likely attribute causes of problems to controllable factors. This may lead to the assumptions that PWE may be more responsible for their symptoms and comorbidities and therefore increase negative attitudes and discriminating behaviors. Thus, this might have been another possible mechanism why perceived stigma was increased in higher SES districts in our study.

Other correlates

Perceived restrictions of everyday life were the most important predictor of stigma in our model. The (univariate) correlation was similar to that from a previously identified correlation (24). Our finding is also in line with theoretical models suggesting that problems in everyday social domains, e.g., with family and friends, leisure time activities or education and employment, may lead to feelings of higher stigma (19). However, causal conclusions cannot be drawn from our cross-sectional analysis. Therefore, the observed association may also represent effects in the opposite direction, i.e., detrimental effects of perceived stigma on social everyday functioning.

Moreover, patients who were seizure-free in the past 6 months reported more stigma. This finding is counterintuitive and somewhat unexpected as it contradicts previous research (11). In the public, seizures represent the key characteristic of epilepsy and are surrounded by many stigmatizing false beliefs (47). Thus, it may be reasonable that seizure freedom leads to less perceived stigma. However, our contrary finding may be due to the fact that seizure freedom does not mean that PWE may not suffer from other epilepsy-related problems, for instance cognitive problems, depressive symptoms or ASM adverse effects (48–50). All study participants were in-patients of the epilepsy center. Thus, also those who were seizure-free needed medical treatment due to conditions limiting their health. Possibly, these problems may be even greater sources of stigma than seizures themselves. Public stereotypes beyond seizures regarding PWE include that they are seen as over-anxious, antisocial, aggressive or retarded (47). Thus, PWE suffering from anxiety, behavioral or cognitive complaints may identify themselves stronger with these perceptions which may increase perceived stigma.

Is the SES relevant for stigma?

In their systematic review, Baker et al. (45) summarized studies showing that the association between individual SES characteristics and stigma disappeared after controlling for psychological variables such as depression or QoL. Therefore, they concluded that the association between an individual person's SES and stigma rather reflects overlap between SES and other psychological variables. However, in contrast to this explanation, we found that individual as well as structural SES were more important in predicting perceived stigma than other demographic, clinical and psychological variables. We did not identify relevant multicollinearity of psychological and SES variables. Moreover, even after re-entering "QoL," "depressive symptoms" and "anxiety symptoms" as possible predictors, stigma was still significantly associated with "SI district," "SI neighborhood" and "unfavorable income." Three of five predictors in the final model were related to the individual or structural SES, and they explained 7.7% of the variance of stigma. What is more, the variable "restrictions of daily life," the most important predictor of stigma, represents a patient-rating of social everyday functioning. Thus, it may be seen as a social correlate in the broader sense. All in all, our findings indicate that social variables on different levels represent important correlates of perceived stigma and that they, at least in our sample, are even more important than psychological characteristics.

Clinical consequences and stigma reduction strategies

Our finding of a negative association between "SI neighborhood" and perceived stigma may reflect that the immediate living environment of PWE in socially deprived neighborhoods offers fewer resources for social support or for developing coping abilities. In these areas, patient-based interventions to enhance social competencies, self-esteem, coping and epilepsy knowledge (51) may be less available for PWE and their caregivers. As epilepsy often leads to reduced mobility, especially in deprived areas, psychosocial and psychoeducational interventions should be installed.

In addition to individual interventions, public awareness interventions are relevant all over the city. For instance, lectures, entertainment events, or public service announcements, should be used to increase knowledge about epilepsy in the general population and also in PWE themselves (51). Our non-linear association between "SI district" and stigma leads to the conclusion that the programs should not specifically focus on regions of higher or lower SES. Instead, the programs should be targeted according to the specific needs in the districts. Cultural-specific interventions could make use of cultural diversity in districts of lower SES. Moreover, higher SES districts could improve prevention of stigma by providing specific information on controllability of epilepsy and its comorbidities. School-based interventions should also cover these aspects in order to educate children, adolescents and their families early.

Our results further suggest that psychotherapy should regularly include the possible stigma of epilepsy. We found moderate to high correlations of depressive symptoms and anxiety symptoms with stigma (Table 2), suggesting that PWE seeking therapy due to these comorbidities may especially suffer from stigma. Therapists should create settings to allow for correcting relationship experiences. Therefore, information about epilepsy should be provided in psychotherapists' training to reduce their possible epilepsy-related restraints and stereotypes.

Limitations, generalizability and further research

Due to the cross-sectional nature of our study, we cannot draw conclusions about the directions of the observed relationships. Longitudinal and qualitative research is needed to gain further insight in possible causal mechanisms. Moreover, we only focused on the patients' perception of stigma, i.e., rather subjective views of "felt stigma." In addition to that, the concept of "enacted stigma" refers to actual episodes of discrimination, e.g., bullying due to epilepsy, representing a more objective perspective. For a comprehensive view on stigma and its everyday life consequences, both aspects should be taken into account in further studies. Our sample consists of patients from 2018 to 2021 whereas the latest version of the measures for structural SES, the social indices of Berlin, was published in 2013. However, the SIs of different periods (e.g., 2008 and 2013) are usually highly correlated (37, 52), so that if any, only a small bias due to changes of the social structure of Berlin in our results is expected. Moreover, our in-patient sample may have suffered from particularly severe epilepsies, and to draw conclusions about a more representative epilepsy population, outpatient settings should be examined as well. Finally, comparisons with other cities and countries are needed to examine whether our results were specific to Berlin and/ or Germany.

Moreover, a possible limitation of our study is that we did not include a control group. Additional research is needed to test whether our findings are generalizable to other chronic health conditions. For example, HIV-related or mental health stigma also showed associations with the structural SES in previous studies (16, 43). However, whether stigma against other conditions also differs even according to different regional levels within one city, needs to be proven. Directly comparing groups of different chronic medical illnesses with respect to the relations between SES and stigma may give additional insight in underlying mechanisms and treatment needs. Prevention and intervention programs may greatly benefit from the corresponding findings.

Stigma may play an important role for pathological social stress in urban populations. Our findings suggest that structural socioeconomic conditions of the living environment should be considered within this framework. However, our non-linear relationships indicate that at least some indicators of lower structural SES may not cause higher stigma levels. These findings may be particularly important within the interdisciplinary field of neurourbanism. Further research is needed to disentangle the mechanisms from an interdisciplinary perspective. For instance, instead of using a composite measure of SES, studies could investigate specific aspects of the residence, e.g., average household income rates, educational qualifications, cultural diversity and also the nature outdoor environment and green space (22, 43, 53). This may help to identify possible resilience factors in areas with lower structural SES.

Conclusion

We found that the social structure of the residence was linked to perceived stigma in patients with epilepsy in Berlin. Interventions to reduce and prevent epilepsy-related stigma already exist but regarding their efficacy, outcomes are mixed (51). These patient-based and public interventions should take

into account that perceived stigma varies according to the social environment and may, therefore, be improved taking into account different regional needs. All in all, our findings regarding epilepsy-related stigma may be transferred to stigma against other health conditions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board of Charité–Universitätsmedizin Berlin. The patients/participants provided their written informed consent to participate in this study.

Author contributions

LH collected and analyzed the data, together with MH she wrote the manuscript. S-UK and JB contributed to data collection and reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

Author MH received speaker's honoraria and/or consultancy fees from Angelini, Bial, Desitin, Eisai, GW Pharmaceuticals, Neuraxpharm, UCB, and Zogenix.

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Publisher's note

Supplementary material

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Family functioning and delinquency among Chinese adolescents: Mediating effects of positive behavior recognition according to the humanistic perspective

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Background: Empirical research on the relationship between family functioning and delinquency has been sparse, although many studies have focused on the influence of family functioning on adolescent development. The current research aimed to fill this gap by exploring the influences of family functioning on adolescent delinquency and the mechanisms connecting the processes.

Methods: We derived the baseline data from a prospective observational school-based cohort Chengdu Positive Child Development (CPCD) project. Students responded to a questionnaire containing validated measures of family functioning, positive behavior recognition, and delinquent behavior. We utilized structural equation modeling and maximum likelihood estimation to test the relationships.

Results: Across 8811 Chinese adolescents, the incidence of delinquency behaviors among Chinese adolescents was relatively low. Family functioning and positive behavior recognition negatively predict delinquency ($p < 0.001$). Further, positive behavior recognition partially mediated the influence of family functioning on delinquency [$p < 0.001$, std. error = 0.01, 95% CI = (0.04, 0.07)]. Adolescents with better family functioning had little delinquency behavior, with positive behavior recognition and delinquency behavior negatively reinforcing each other.

Conclusions: This study demonstrated that family functioning was a protective factor against adolescent delinquency and revealed that positive behavior

recognition was a critical mediating mechanism linking family functioning to delinquency.

KEYWORDS

Chinese adolescents, delinquency, family functioning, humanistic perspective, mediator, positive behavior

Introduction

Behavioral problems refer to abnormal behaviors that exceed the normal range for the corresponding age in terms of severity and duration (1). Delinquency is a behavioral problem defined as engaging in antisocial behavior (2). Adolescence is a critical period of life development and a transition period characterized by physical, psychological, and social changes when adolescents learn to live independently (3). If adolescents cannot adequately cope with these developmental challenges, problematic behaviors such as delinquency likely emerge (4). Abundant evidence has revealed that delinquency is a growing global concern due to its high incidence, especially among early adolescents in both Western and Chinese backgrounds (5). For example, a representative sample study ($N = 4{,}0502$) showed that 46% of adolescents in Grade 7 to 12 in the United States engaged in offending behaviors (5). The studies conducted in Asia, such as in China and South Korea, have shown a relatively low but still significant prevalence of adolescent delinquency (6, 7). A large cross-sectional study reported that the total detection rate of behavioral problems in two districts in Beijing was 16.7% (8). A statistical report on China's Youth Development (2020) jointly released by the China Youth and Children Research Center and the International Liaison Department of the Central Committee of the Communist Youth showed that the number of criminals under 18 is rising (9).

Delinquency has been associated not only with poor outcomes such as alcohol and drug abuse and mental health problems (10–12) but also linked to long-lasting consequences (13), including severely hindering interpersonal development and even social sustainability (14, 15). Early and persistent delinquent acts strongly predicted violent behavior, partner conflict, unemployment later in adolescence (16, 17), and chronic antisocial behavior (18). Given its high prevalence and long-term disruptive outcomes, adolescent delinquency undoubtedly has become a severe social problem that has brought stress and high costs to families and society (19). Thus, identifying the predictive and protective factors for delinquency becomes an essential task of youth studies that could contribute to adolescent health programs.

The family environment is vital to the individual's psychological behavior (20). Family functioning refers to a model in which family members can obtain the necessary material and spiritual conditions to advance and promote their physical, mental, and social development in a healthy and beneficial direction (21). Although many theories and studies (22, 23) suggest that when an individual enters adolescence, his/her focus shifts from family and parents to peers, numerous studies have found that family still profoundly influences adolescents (24, 25). Bronfenbrenner proposes five environmental systems based on the ecosystem theory (1979), from the most private to the most general environment: microsystem, mesoscopic system, external system, macrosystem, and temporal system. Family and peers are the critical microsystem variables that influence an adolescent's risk-taking behavior (26). Family functioning is critical in evaluating the family environment, including role assignment, communication, emotional response and intervention, effective problem-solving ability, and behavior control (27). Psychologists and sociologists stress the importance of parental and positive parent-child relationships for children's growth and development (28, 29). Good family function includes high levels of love and support, positive communication, and behavioral discipline (30), providing positive emotional experience and cognitive attitude for individuals, promoting individual mental health (31) and good adaptation (32), and reducing the incidence of problem behavior (26). However, poor family functioning, such as parent-child conflict and marital conflict between parents, damages adolescents' psychological resources and leads to various problem behaviors (33). Although many studies have explored the influence of family functioning on adolescent development, few scholars in China, except Shek (4, 34, 35), have explored the protective effect of family function on adolescent delinquency and explained the negative correlation with delinquency from the dimension of family functioning. Based on this discussion, we proposed Hypothesis 1: Family function can negatively predict delinquency in Chinese adolescents.

Positive behavior includes visible skills that increase the likelihood of success and personal satisfaction in normative academic, work, social, recreational, community, and family settings. The term "positive behavior" can be seen as equivalent to "prosocial behavior" (36). Positive behavior recognition is the appropriate response of the social environment to such behavior (37). The goal of recognition is to encourage adolescents to continue exhibiting positive behavior. Some researchers have proposed that positive behavior recognition is related to the positive self-perception of adolescents and can

increase their likelihood of positive and prosocial behavior (36). Therefore, positive behavior recognition is an essential internal psychological resource for adolescent development. Studies have shown that a high level of identification can effectively reduce adolescent Internet addiction, emotional disorders, and other problem behaviors (38). However, few studies have explored the relationship between positive behavior recognition and delinquency. Thus, we hypothesized that positive behavior recognition significantly and negatively predicts delinquency (Hypothesis 2).

Some studies have confirmed that good family function can positively predict adolescent positive behavior recognition (38–40). A study of 148 adolescents living in the Netherlands with an average age of 15 showed that good maternal communication facilitates adolescents' search for positive behavior identification (40). However, few studies have explored the association between family functioning and positive behavior recognition among Chinese adolescents. Therefore, we hypothesized that family functioning positively predicts Chinese adolescents' positive behavior recognition (Hypothesis 3).

According to the humanistic view, positive behavior signifies positive human development. Rogers, a key figure in humanistic psychology, proposed a theory closely related to positive behavior recognition. According to Rogers (41), unconditional positive respect is one condition that leads to healthy relationships. Unconditional positive respect is when one maintains an unconditional, positive attitude toward others that gives the recipient a sense of self-worth. Positive behavior identification through personal warmth can be an aspect of positive respect. In addition, a significant other's recognition of a child's or adolescent's good deeds through warm and supportive verbal and non-verbal gestures can kickstart an individual's internal organizational enhancement, turning the individual into a better person in the whole process. In this way, unconditional positive respect is critical to human functioning as a form of positive behavior recognition.

There is research on family functioning, positive behavior recognition, and delinquency behaviors. Although some studies have found links between marital discord, parenting, parental attachment, and adolescent delinquency, the underlying mechanisms behind these associations are unclear (42). The family environment has an important influence on individual psychological behavior. Because positive behavior recognition has been considered an essential personal protective resource, few researchers have examined the relationship between family functioning, positive behavior recognition, and delinquency. They rarely discussed the mediating role of positive behavior recognition from a humanistic perspective. Thus, we formulated our hypothesis: Positive behavior recognition is a mediator in the influence of family functioning on adolescent delinquency (Hypothesis 4).

Although there have been many empirical studies on the relationship between family function and adolescent delinquency in the West, whether the conclusions of this study could explain part of the family factors affecting juvenile delinquency in China is not certain. Although many researchers in China have realized that family functioning plays a vital role in influencing adolescent delinquency, few empirical studies have examined the relationship between family functioning and adolescent delinquency. This study aimed to fill the knowledge gap. Based on Rogers' Humanistic Perspective, we predicted that teenagers in a good family functioning environment might have a high level of concern and support, good communication and behavior, discipline, and unconditional positive respect. Therefore, their good deeds are more likely to be identified to enhance the internal organization, recognize positive behavior, increase prosocial behavior, and reduce delinquency.

Some studies on the prevention of adolescent problems suggest that prevention should focus on reducing and preventing problems, but this is a "pathological" approach and limits the public's understanding of the personal potential of adolescents (43). Adolescents are not "troubles" but valuable resources with abilities, potentials, and strengths that can be cultivated and utilized to promote their overall development and active functioning (44). Therefore, the present study aimed to identify and add another internal personal resource to protect adolescents from problem behaviors, hoping to contribute to developing adolescent health programs. However, other problems exist, such as the single research method, small sample size, and lack of high reliability and validity measurement tools. Moreover, the family factors influencing adolescent delinquency are very complex. Based on the humanistic perspective, we hope our study can provide Chinese data by carrying out a large sample empirical study in the context of Chinese culture.

Based on the above four assumptions, the present study proposed a mediation model as the conceptual framework of the present study (see Figure 1). A previous study has found that age and gender were associated with family functioning and adolescent delinquency (45). Hence, we included these demographic variables as control variables in this study.

Materials and methods

Participants

We derived the baseline data from a prospective observational school-based cohort Chengdu Positive Child Development (CPCD) Project, launched in December 2019 in Chengdu, the capital of Sichuan province. The CPCD Project aimed to investigate the current state of positive development and psychosocial and behavioral problems in children. The

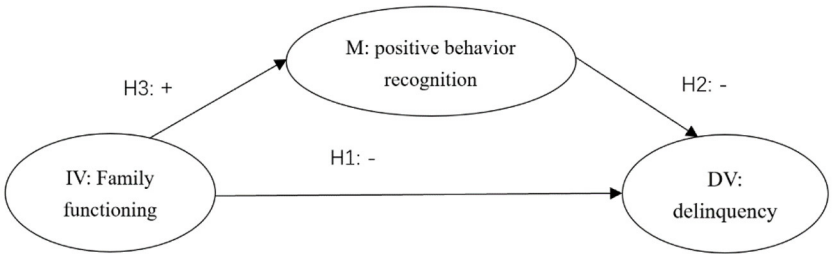

FIGURE 1
Hypothesized association among family functioning attributes, positive behavior recognition, and adolescent delinquency. IV, independent variable; M, mediator; DV, dependent variable.

researchers adopted cluster and convenience sampling methods to select five primary and middle schools: one downtown, two in the suburbs in the south, and two in the north of Chengdu. All data are available (see Data Availability statement). The student's legal guardians gave written informed consent prior to participation. The informed consent included a project overview, survey procedures, potential benefits and risks, and a confidentiality agreement. The Medical Ethics Committee approved the study protocol of Sichuan University (K2020025).

Investigative procedures

The project sent the questionnaires as the baseline survey. Students in Grades 1–9 who attended school on the survey date filled in the questionnaire.

Collection and non-response bias are two common types of bias in cross-sectional surveys. Some studies showed no significant difference between the paper-based and online collection methods (46). In addition, self-reported data may be susceptible to social desirability bias as the respondents may tend to provide answers perceived as more socially acceptable. A self-administered questionnaire could reduce the social-desirability bias (47) if the survey questions were sensitive. A lower response rate can easily cause researchers to worry about non-response bias. Transparent and organized paper-based questionnaire items could help participants answer questions quickly to reduce low responses.

Therefore, considering the feasibility of investigating primary schools, we took the following measures to ensure the authenticity and completeness of the information the students filled in.

First, we devised a paper-based and self-administered questionnaire with transparent and organized survey items. Second, we created a quiet and comfortable environment and provided the students plenty of time (40∼60 min), and no one was allowed to submit in advance. All students independently completed the questionnaire under the supervision of the head teacher and investigators. Before the study began, the students could ask trained teachers questions when they had problems rather than discuss them with each other. Third, we used some negative scoring items in the questionnaire for logical checking. Finally, we collected the questionnaires on the spot, reviewed them, and promptly corrected them if there were any problems, such as missing data. Questionnaires with logical errors were excluded (For example, a questionnaire in which the respondents offered obvious contradictory answers was excluded).

Measures

Assessment of family functioning

The Chinese Family Assessment Instrument (C-FAI) is a 33-item self-report scale developed to assess family functioning (48). The C-FAI has five subscales, including mutuality (mutual support, love, and concern among family members) (12 items), communication (frequency and nature of interaction among family members) (9 items), conflict and harmony (conflicting and harmonious behavior in the family) (6 items), parental concern (parental support behavior) (3 items), and parental control (harshness of parenting behavior) (3 items). Items include statements such as "Parents often talk to their children," "Family members care about each other," and "There is a lack of harmony among family members." For each item, there is a five-point Likert scale (1 = very similar; 2 = somewhat similar; 3 = between somewhat similar and somewhat dissimilar; 4 = somewhat dissimilar; 5 = very dissimilar). Higher scores reflect greater dysfunction within the family. A previous study has confirmed that the C-FAI was a valid and reliable measure of family functioning (Cronbach's $\alpha = 0.933$) (49). Our study also showed good reliability in delinquency (Cronbach's $\alpha = 0.936$).

Assessment of delinquency

We used a 12-item 7-point scale to assess the occurrence of delinquent behaviors of the participants in the past year (50). For each item, there is a six-point scale (0 = never, 1 = one to two times; 2 = three to four times; 3 = five to six times;

4 = seven to eight times; 5 = nine to ten times; 6 = more than ten times). For complete scale information, please refer to Appendix A. A higher score on this scale denoted a greater degree of delinquency. This scale demonstrated good validity and reliability in the previous two studies (α = 0.76, α = 0.88, respectively) (50, 51). Cronbach's alpha in this study was 0.835.

Assessment of positive behavior recognition

We selected the Recognition for Positive Behavior subscale (PB) (51) from the Chinese Positive Youth Development Scale (CPYDS) designed by Shek et al. (5). There are four items in the subscale. The items were developed after reviewing the literature (52) and discussing between the first two authors. For each item, there is a six-point scale (1 = strongly disagree; 2 = relatively disagree; 3 = slightly disagree; 4 = slightly agree; 5 = relatively agree; 6 = strongly agree). For complete scale information, please refer to Appendix B. Higher scores on this scale indicated greater positive behavior recognition. The previous study has shown the scale had good validity and reliability (α = 0.76 and 0.80 at pre-and post-test) (53). Cronbach's α for this scale in our study was good (α = 0.772).

Data analysis

We used the EpiData 3.1 (EpiData Association, Odense, Denmark) for double data entry and logic error verification. We used student's *t*-test to compare continuous variables (age, body mass index [BMI]) and the Mann–Whitney U test to compare non-normally distributed continuous variables (family functioning, positive behavior recognition, delinquency). To compare categorical variables (sex), we used the Chi-square test. Any *P*-values <0.05 were considered statistically significant.

To test the hypothetical models depicted in Figure 1, we performed the structural equation model in R version 4.1.3 with packages lavaan and semplot, using maximum likelihood estimation with robust standard errors. We performed the structural equation modeling analysis in two steps: (i) We examined the total effect of family functioning on positive behavior recognition and delinquency; (ii) We examined the direct and indirect effects of family functioning on delinquency, considering positive behavior recognition as a potential mediator. We considered that the adolescents' positive behavior recognition might display diversity due to their different ages, sex, and BMI. Therefore, age, sex, and BMI were included in the model to correct these effects on adolescents' positive behavior recognition.

In order to facilitate the interpretation of model results and the comparison of effect values, we multiplied the score of C-FAI by −1 to keep all correlations in the same direction. In addition, we assessed the overall fitting performance of the model by using the Comparative Fit Index (CFI), normed fit index (NFI), non-normed fit index (NNFI), and root mean square error of approximation (RMSEA) and other indicators. Generally speaking, CFI, NFI, and NNFI values >0.9 and RMSEA values <0.08 are considered good model fit indices (54). However, the cut-off value of the structural equation model fit indices is always controversial. MacCallum et al. proposed that an RMSEA of between 0.08 to 0.10 provides a mediocre fit and below 0.08 shows a good fit (55). The cut-off as low as 0.80 has been proferred; however, Bentler and Hu have suggested NNFI ≥ 0.95 as the threshold (56).

Results

Descriptive statistics

We sent out a total of 8,968 questionnaires during the baseline survey, and a total of 8,811 students in Grades 1–9 (aged 6–16) who attended school on the survey date have completed the questionnaire, with a response rate of 98.4%. There were slightly more boys than girls (51.6 vs. 48.4%) and more primary than middle school students (62.7 vs. 37.3%). More students lived in urban than rural areas (65.0 vs. 35.0%). Moreover, the average age of boys and girls is 12.86 ± 2.33 and 12.90 ± 2.32, respectively.

The detection rate of delinquency behavior

Results in Table 1 show that delinquency behaviors were relatively low among Chinese adolescents. More than 90% of the respondents reported that they had never stolen, fought in a gang, or had a sexual relationship with others (other than assault and damaging others' properties) in the past year. In contrast, about half of the respondents reported having cheated on somebody or spoken foul language.

Descriptive statistics of the participants on delinquency, family functioning, positive behavior recognition

Table 2 indicates boys scored significantly higher on delinquency than girls ($t = 11.24$, $P < 0.001$). Boys also scored higher on family functioning than girls ($t = 3.44$, $P < 0.001$), indicating boys have higher family dysfunction levels than girls. However, boys scored lower on positive behavior recognition than girls ($t = -3.79$, $P < 0.001$).

TABLE 1 Summary table of the reported frequency of delinquency behavior ($N = 8,811$).

Delinquency	Never (%)	1–2 times (%)	3–4 times (%)	5–6 times (%)	7–8 times (%)	9–10 times (%)	>10 times (%)	Mean times
Stealing	91.38	6.56	1.16	0.19	0.14	0.80	0.50	0.13
Cheating	57.82	26.75	8.73	2.742	0.86	0.49	2.61	0.74
Truancy	96.57	1.99	0.61	0.30	0.17	0.03	0.33	0.07
Running away from home	93.12	4.81	0.90	0.53	0.15	0.09	0.41	0.12
Damaging others' property	87.72	9.24	1.65	0.59	0.24	0.11	0.45	0.19
Assault	87.15	8.91	1.80	0.79	0.32	0.23	0.81	0.22
Having a sexual relationship with others	93.81	3.94	0.87	0.48	0.26	0.16	0.48	0.12
Gang fighting	94.07	3.77	0.87	0.42	0.19	0.20	0.47	0.11
Using foul language	46.43	28.28	9.27	4.42	1.80	0.96	8.85	1.25
Staying away from home without parental consent	94.88	3.00	0.91	0.42	0.24	0.08	0.48	0.10
Strong-arming others	90.26	6.41	1.46	0.70	0.31	0.22	0.65	0.18
Breaking into residences	95.80	2.65	0.53	0.31	0.14	0.20	0.37	0.08

TABLE 2 Descriptive statistics of the participants on delinquency, family functioning, and positive behavior recognition.

Variables	Boys ($N = 4,543$)					Girls ($N = 4,268$)						
	Min	Max	Mean	Variance	SD	Min	Max	Mean	Variance	SD	Test value	*P*-value
Family functioning	31	155	56	549.95	23.45	31	155	35	522.26	22.85	3.44	<0.001
Mutuality	6	30	10.68	28.53	5.34	6	30	10.48	26.39	5.14	1.84	0.07
Communication	5	25	9.61	27.38	5.23	5	25	9.76	26.38	5.14	−1.27	0.20
Conflict and harmony	10	50	20.07	70.68	8.41	10	50	19.55	65.97	8.12	2.96	< 0.01
Parental concern	7	35	13.23	46.82	6.84	7	35	12.62	39.74	6.3	4.34	<0.001
Parental control	3	15	6.91	13.08	3.62	3	15	6.41	11.58	3.4	6.73	<0.001
Positive behavior recognition	4	24	20.03	16.51	4.06	4	24	20.35	13.58	3.69	−3.79	<0.001
Delinquency	0	72	3.98	50.63	7.12	0	59	2.59	17.64	4.2	11.24	<0.001

Correlations among variables

Table 3 shows the correlations among variables. Family functioning was negatively related to delinquency ($r = -0.28$, $P < 0.001$). The four dimensions of Family Functioning (mutuality, communication, conflict and harmony, and parent concern) had a relatively higher correlation ($r = -0.25$, $r = -0.25$, $r = -0.24$, $r = -0.23$, $P < 0.001$, respectively) to delinquency than parent control ($r = -0.13$, $P < 0.001$). Positive behavior recognition was negatively related to delinquency ($r = -0.21$, $P < 0.001$). Family functioning was positively correlated with positive behavior recognition ($r = 0.34$, $P < 0.001$). Overall, these observed results are consistent with our original hypotheses.

Predictions of delinquency and mediating effect of positive behavior recognition

Model testing

The model assessment showed an acceptable model fit. The results were $\chi^2 = 2,533.635$, df = 31, CFI =0.896, NFI = 0.895,

TABLE 3 Intercorrelation matrix for family functioning variables, positive behavior recognition, and delinquency.

Variables	1	2	3	4	5	6	7	8	9	10	11
1. Family Functioning	—										
2. Mutuality	0.85**	—									
3. Communication	0.80**	0.76**	—								
4. Conflict and harmony	0.90**	0.67**	0.60**	—							
5. Parent concern	0.84**	0.59**	0.55**	0.72**	—						
6. Parent control	0.46**	0.30**	0.20**	0.32**	0.28**	—					
7. Recognition of positive behavior	0.34**	0.29**	0.26**	0.30**	0.28**	0.21**	—				
8. Delinquency	−0.28**	−0.25**	−0.25**	−0.24**	−0.23**	−0.13**	−0.21**	—			
9. Gender	0.04*	0.02	−0.01	0.03*	0.05**	0.07**	0.04*	−0.12**	—		
10. Age	−0.01	0.01	−0.03	−0.02	−0.03*	0.07**	−0.17**	0.13**	0.01	—	
11. BMI	−0.01	0.01	−0.01	−0.01	−0.01	0.03	−0.08**	0.07**	−0.02	0.44**	—

**$p < 0.001$, *$p < 0.05$. Minor correlation when $0 \leq R < 0.2$, slight correlation for $0.2 \leq R < 0.4$, moderate correlation for $0.4 \leq R < 0.7$, and high correlation for $0.7 \leq R \leq 1.0$.

NNFI = 0.859, RMSEA = 0.096 [95% CI = (0.093, 0.096)]. More information about the Model fit is in Appendix C.

Testing of mediation effects

Figure 2 outlines the standardized path coefficients and path significance of the relationships between family functioning, positive behavior recognition, and delinquency. First, family functioning ($\beta = -0.26$, $P < 0.001$) negatively predicted adolescent delinquency, supporting Hypothesis 1.

Second, positive behavior recognition showed negative predictive effects on adolescent delinquency ($\beta = -0.12$, $P < 0.001$), supporting Hypothesis 2.

Third, Family functioning positively contributed to positive behavior recognition ($\beta = 0.35$, $P < 0.001$), supporting Hypothesis 3.

Table 4 presents the path coefficients and the decomposition of effects in the structural mediation model. When using positive behavior recognitions as the mediator, the indirect effects of family functioning on delinquency were also significant, supporting the mediating effect model [$\beta = -0.04$, $b = -0.06$, 95% CI = $(-0.07, -0.04)$, $P = 0$]. Overall, the mediation model explained 10.1% of the variance in delinquency.

Discussion

Family functioning negatively predicts adolescent delinquency

Regarding our first research question, correlation and regression analyses consistently revealed that family functioning could negatively predict adolescent delinquency. Adolescents with better family mutuality, communication, parental concern, and fewer family conflicts had less delinquency behavior. These findings supported our initial hypothesis 1. These results are also consistent with the findings of other studies (34, 35, 57, 58). A positive and supportive family environment could reduce delinquent behavior because children who received warm care from their parents were more likely to conform to rules and develop positive behavior (59, 60).

As adolescents grow up, they relate to non-family members such as their peers (61); more family conflicts and poor family communication might even push them to seek non-familial support (57). The difficulties children have experienced at home are then carried over into school life and peer relationships, resulting in disrupted relationships with mainstream peer groups. To regain a sense of membership, those individuals whom conventional peers reject may join delinquent peer groups and have their antisocial behaviors reinforced (35). Previous studies have shown that parental control and concern (parental support behavior) effectively reduce adolescent conduct problems (62–65). Authoritative parenting is conducive to establishing a positive parent-child relationship, facilitating children's open communication with parents, enhancing parents' ability to identify potential risks children may encounter, and intervening when necessary (66). However, the correlation between parent control and delinquency in the present study was relatively low compared to the other four dimensions of family functioning, as shown in Table 3. This may suggesting that parental control is less important than the other four factors, further strengthening other four aspects of family functioning may increase the extent to which family functioning contributes to adolescent delinquency.

In general, the findings are congruent with the family systems theory expectation that the development of family function attributes provides the essential external

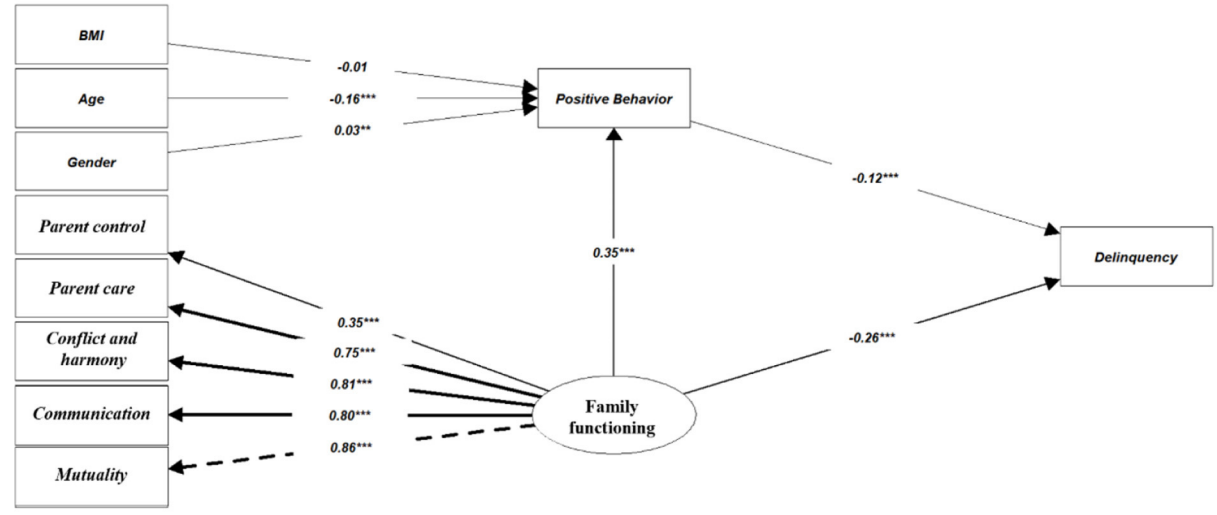

FIGURE 2
Standardized path coefficients for the relationship between family functioning, positive behavior recognition, and delinquency. $^{***}p < 0.001$, $^{**}p < 0.01$.

TABLE 4 Presents the path coefficients and indirect effects of family functioning on delinquency.

Variables	Standardized regression coefficient	beta	Std. error	z	P-value	95% CI lower	95% CI upper	R^2	f^2
Measurement model									
Family functioning (FF)→ Delinquency	−0.26	−0.34	0.03	−12.94	0	−0.39	−0.29		
FF→ Positive behavior recognition (PB)	0.35	0.30	0.01	25.28	0	0.28	0.32	0.147	0.172
PB → Delinquency	−0.12	−0.19	0.02	−7.63	0	−0.23	−0.14		
Structural model									
Direct FF→ Delinquency	−0.26	−0.34	0.03	−12.94	0	−0.39	−0.29		
Direct PB→ Delinquency	−0.12	−0.19	0.02	−7.63	0	−0.23	−0.14		
Indirect FF→ PB→ Delinquency	−0.04	−0.06	0.01	−7.37	0	−0.07	−0.04		
Total FF→ PB→ Delinquency	−0.42	−0.58	0.03	−20.25	0	−0.63	−0.52	0.101	0.112

resources to protect adolescents from delinquency. The current findings broaden existing family function literature by including an Asian sample, further extending the conclusion to China mainland, suggesting that the general negative relationship between family functioning and delinquency may hold for different cultural contexts.

Positive behavior recognition serves as a mediating factor

Consistent with previous studies, our findings showed that family functioning was positively related to positive behavior recognition, and both were inversely associated with delinquency. These findings also supported Hypotheses 2 and 3.

These results are consistent with those of other studies (38–40, 43, 67–69).

For the fourth research question, the overall findings also support our hypothesis that positive behavior recognition is a mediator predicting the effect of family functioning on delinquency.

According to the humanistic theory, human behavior and experiences are guided by one essential striving in life: the fundamental tendency to develop all capacities to enhance the person's functioning, thereby generating positive behavior (70). All urges, desires, wants, goals, values, and motives are subsumed under "organismic enhancement." A person will become all that he or she can become with his or her potential fulfilled. According to Rogers, one interpersonal condition that leads to healthy development is unconditional positive regard, which is essential to healthy development. The absence of this condition may lead people to view themselves negatively. Human services professionals believe that giving people unconditional positive regard and acceptance provides the best possible conditions for personal growth (41). Good family functions, such as the harmonious relationship between parents, harmonious communication between parents and children, and family cohesion, are critical for adolescents to gain positive identity and unconditional acceptance (71).

Based on Rogers' Humanistic Perspective, adolescents in a well-functioning family environment receive a high level of parental concern and support, maintain good family mutuality, communication, and behavioral discipline, and are more likely to receive unconditional positive respect. Therefore, their good deeds are more likely to be recognized, activating their internal organizational enhancement and making positive behavioral identifications to increase prosocial behavior and reduce delinquency.

Overall, the findings suggest that family functioning enables adolescents to present more positive behavior recognition, leading to a lower delinquency level.

Based on the current results, cultivating inner strengths (such as positive behavior recognition) for Chinese adolescents is a promising strategy to promote adolescents' well-being and protect them from delinquency. In addition to adopting positive behavior recognition through good family functioning, instructors are also encouraged to inject the meaning of positive behavior during various activities throughout the program implementation in primary schools. Adolescents are an essential part of the urban population, and their physical and mental health is also the focus of the government, school, and family. This study also provides data on the adolescent population for urban population health research.

Strengths and limitations

This study adds to the few related studies in this area, particularly in the Chinese context. It is the first study to add theoretical and practical value to the existing literature by deepening our understanding of the mediating role of positive behavior recognition from a humanistic perspective. A second strength is that the present study also attempts to identify internal personal resources to protect adolescents from problem behaviors that would contribute to developing adolescent health programs. A third strength is that there are few related studies in Chinese contexts, so we recruited Chinese adolescents for the present study. A final strength is the large sample size.

A limitation of this study is the cross-sectional design. In order to conclude the causal relationship between the study variables, further prospective studies are needed. Second, as the present model is based on a large sample collected in Chengdu, mainland Chinese, the generalizability of the findings to adolescents in other Chinese cities remains unknown at this stage. Therefore, future studies should replicate these results to test our findings' generalizability. Third, the model fit is acceptable in the present study. However, there are specific percentages of unexplained variance in the model, which indicates that other potential variables should be included in the model to give a higher degree of prediction. Focus on other inner personal resources could be the future research topic.

Fourth, we collected the data through students' self-reporting, which might increase the likelihood of reporting bias. However, we chose self-administrated paper surveys and collected the questionnaires on the spot, which reduced this problem. In addition to including the reporting data from parents and teachers, future research could consider using methodological approaches, such as multidimensional item response theory and responder misclassification correction formulas (72, 73), to analyze the self-reported outcome bias.

Conclusions

Our survey methodology was feasible, understandable, and helpful in providing data on the prevalence of delinquency in Chinese adolescents. This study demonstrated that family functioning was a protective factor against adolescent delinquency and revealed that positive behavior recognition was a critical mediating mechanism linking family functioning to delinquency. The present findings represent a significant advance in the literature on family functioning and delinquency, particularly in the Chinese context.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The study protocol was approved by the Medical Ethics Committee of Sichuan University (K2020025). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

Conceptualization: XLW and LD. Formal analysis and data curation: SMJ. Investigation: ML and BXH. Funding acquisition, project administration, resources, and supervision: LZ. Writing—original draft: XLW. Writing—review and editing: WS and LD. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.985936/full#supplementary-material

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Cities and neuroscience research: A systematic literature review

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Background: Cities are becoming the socio-economic hubs for most of the world's population. Understanding how our surroundings can mentally affect everyday life has become crucial to integrate environmental sustainability into urban development. The present review aims to explore the empirical studies investigating neural mechanisms underlying cognitive and emotional processes elicited by the exposure to different urban built and natural spaces. It also tries to identify new research questions and to leverage *neurourbanism* as a framework to achieve healthier and sustainable cities.

Methods: By following the PRISMA framework, we conducted a structured search on PubMed, ProQuest, Web of Science, and Scopus databases. Only articles related to how urban environment–built or natural–affects brain activity through objective measurement (with either imaging or electrophysiological techniques) were considered. Further inclusion criteria were studies on human adult populations, peer-reviewed, and in English language.

Results: Sixty-two articles met the inclusion criteria. They were qualitatively assessed and analyzed to determine the main findings and emerging concepts. Overall, the results suggest that urban built exposure (when compared to natural spaces) elicit activations in brain regions or networks strongly related to perceptual, attentional, and (spatial) cognitive demands. The city's-built environment also triggers neural circuits linked to stress and negative affect. Convergence of these findings was observed across neuroscience techniques, and for both laboratory and real-life settings. Additionally, evidence also showed associations between neural social stress processing with urban upbringing or current city living–suggesting a mechanistic link to certain mood and anxiety disorders. Finally, environmental diversity was found to be critical for positive affect and individual well-being.

Conclusion: Contemporary human-environment interactions and planetary challenges imply greater understanding of the neurological underpinnings on how the urban space affects cognition and emotion. This review provides scientific evidence that could be applied for policy making on improved

urban mental health. Several studies showed that high-quality green or blue spaces, and bio-diverse urban areas, are important allies for positive neural, cognitive, and emotional processes. Nonetheless, the spatial perception in social contexts (e.g., city overcrowding) deserves further attention by urban planners and scientists. The implications of these observations for some theories in environmental psychology and research are discussed. Future work should take advantage of technological advancements to better characterize behavior, brain physiology, and environmental factors and apply them to the remaining complexity of contemporary cities.

KEYWORDS

urban science, built environment, natural environment, neuroscience, brain research

Introduction

Over the past few centuries, cities have become the cultural and political centers of most societies, and the scaffolding supporting changes in human desires, needs, and challenges (1, 2). In 2018, more than half of the world's population lived in urban areas and it is estimated that by 2050 the number will rise to around two-thirds (3). Such urbanization phenomenon is, as endorsed by the United Nations General Assembly (4), one of the twenty-first century's most transformative trends. The advantages of living in cities are spread across several socio-economic areas, from a better income and level of employment to a higher education and access to healthcare (5). However, city dwellers also face a vast array of inequalities or environmental changes (e.g., pollution of air and water, transportation problems, reduced social cohesion); and several urban features have direct and/or indirect bearing on human health, physical, and mental (6, 7).

Urban health is a developing discipline concerned with cities' determinants of health and diseases, as well as with the city-living context as an exposure of interest (8)–being a good example of how challenging it could be to achieve sustainable urban development (9, 10). Nonetheless, rather than documenting unhealthy exposures and highlighting the complexity of the human-environment relationship, contemporary urban science examines these interactions at different levels and aims to fully address the causes and mechanisms. This is particularly relevant when studying the interdependence between city life and mental health and wellbeing, where a multi-disciplinary approach–involving biological, socio-economic, infrastructural, and cultural aspects–is crucial (11–15). Despite the vast epidemiological literature emphasizing the association between mental disorders and urban life (16), as well as the advances on how city living and urban upbringing affect the brain processing and associated stress (17), it remains elusive how urban life "gets under the skin" (14).

A person's natural and built environments have a significant effect on the biological processing of cognitive and emotional information. People experience negative (fear, anger, disgust, and sadness) or positive (joy, trust, anticipation, and surprise) emotions while interacting with their surroundings. Research suggests that emotions are the driver of our most important decisions in life; similarly, our cognitive behavioral choices are the conduit for increasing positive emotions or decreasing negative emotions–tendencies associated with well-being (18). Moreover, the impact of cognition and emotions on health is experienced *via* physiological and behavioral mechanisms.

The brain, through complex neural circuits, is at the heart of our homeostatic control and the way we react to environmental stress. It determines what is threatening as well as the behavioral and physiological adaptive responses (19, 20). Neuroscience studies the human brain by focusing either on the effects of pathological changes (e.g., stroke, trauma, or other diseases), or by measuring cerebral activation during a particular behavioral task. The most widely used methodologies are non-invasive and aim to quantify neural activity across brain regions under well controlled conditions. Over the past few decades, we remarkably advanced our knowledge about the neural circuits and basic physiology of cognitive and emotional processing. Concomitantly, we have witnessed a wealth of new technologies, wearable devices, and software applications. Hence, neuroscience has not only moved from classic laboratory-based approaches to more real-world domains (21); but it has also extended its application into a variety of different fields–such as marketing (22), economics (23), and educational (24) sciences.

By recognizing similar potential benefits to the field of urban science, some authors have recently drawn attention to *neurourbanism*–an emerging discipline where theoretical perspectives and analytical methods of basic and clinical neuroscience support urban planning and design practice (11, 12, 25). Addressing the interdependencies between urbanization and neuroscience, it is possible to develop novel theoretical ideas and analytical methods critical for the creation of better city

(built or natural) environments that will improve the mental (and physical) wellbeing of individuals and communities.

A noticeable progress has been made with respect to the link between architecture and the neural mechanisms of spatial navigation (26), aesthetics or design (27, 28). Some of this work aimed to address relevant theoretical formulations, including the cognitive and affective benefits of environmental enrichment (29) and the Appleton's habitat theory (30)–for which an emotionally and aesthetically pleasing environment reflects its favorability to survival. Organizations (31) are promoting the knowledge that links neuroscience research to a growing understanding of human responses to the built environment.

Similarly, it is also paramount to support with neural evidence some prominent environmental psychology theories that aim to explain benefits of exposure to nature, such as the Attention Restoration Theory (ART) (32, 33)–suggesting that natural environments promote recovery from stress and fatigue *via* attention restoration mechanisms; and the Biophilia theory (35)–proposing that brain responses to natural settings reflect more pleasure and relaxation due to an evolutionary benefit of human affinity for nature.

In a systematic review performed a few years ago, Norwood and colleagues (34) explored how different environments affect brain activity and associated mood response. Their results indicate restorative feelings with natural environments and negative affect linked to urban environments. However, their analysis was restricted to mood and emotional processing–leaving cognitive domains aside. Further work (36, 37) also reviewed relevant human-built environment interaction, but their focus was limited to the architectural and interior design settings. In addition, a plethora of new studies have emerged since these reviews. Therefore, there is a clear research need to examine how cognitive neuroscience research has been applied to study the balance between natural ecosystems and built environments in urban areas. Moreover, a contemporary review should also fill a research gap by integrating the emerging evidence about the impact of urban upbringing and current city-living on brain processing.

Here, we aim to provide an up-to-date systematic review of empirical studies investigating the impact of urban built and natural exposure on brain activity and associated cognitive and emotional processes (see **Figure 1**). We explore the wide range of objective brain measurements collected throughout different contexts (in the laboratory or with outdoor real-life experiments), to highlight current explanatory strengths and identify future research needs. With this exercise, we specifically aim to:

1. Provide an up-to-date synthesis of the empirical evidence on how urban exposure and their modulators affect individual brain physiology.
2. Describe the methodologies and contexts that were most used for obtaining such knowledge.
3. Identify emerging concepts and key evidence-based knowledge both scientifically rigorous and capable of informing future research and policy-making agendas.

Methods

The review is reported and follows the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines (38).

Eligibility criteria

We considered all empirical studies written in English published in full-length peer-reviewed journals (abstracts, conference proceedings, and opinion/review articles were excluded but used to search for additional references) until 26th June 2021.

A "Population, Exposure, Comparator, and Outcomes (PECO) approach" (39) was used to define the eligibility criteria. We included studies where brain research methods were applied to human adult populations (healthy or diseased). To be included, studies had to specifically focus on examining how the exposure to urban built or natural environments influenced objective measures of brain activity (exposure duration was not restricted; representations of the environment using virtual reality, pictures or videos were accepted). Comparisons were not specified as criteria, and hence studies (cross-sectional or longitudinal; retrospective or prospective) where participants were exposed to more than two environments or exposed within a context of a randomized or non-randomized trial (e.g., crossover, parallel group, factorial) were considered. Included studies had to provide at least one quantitative outcome measure for brain activity (recorded either pre-, peri-, or post-exposure), either obtained through functional magnetic resonance (fMRI), functional near-infrared spectroscopy (fNIRS), positron emission tomography (PET), electroencephalography (EEG) or magneto-encephalography (MEG). Structural MRI was not included because our focus was on brain activation. Similarly, studies with only psychophysiological measurements (such as heart rate, skin conductance, pupil detection, or eye tracking) do not directly tap into the brain response and, therefore, were also not considered.

Search strategy and information sources

The search strategy involved agreement between our inter-professional team coming from the neuroscience (basic and clinical) as well as urban planning and design fields. Four electronic databases were searched: PubMed, ProQuest, Web

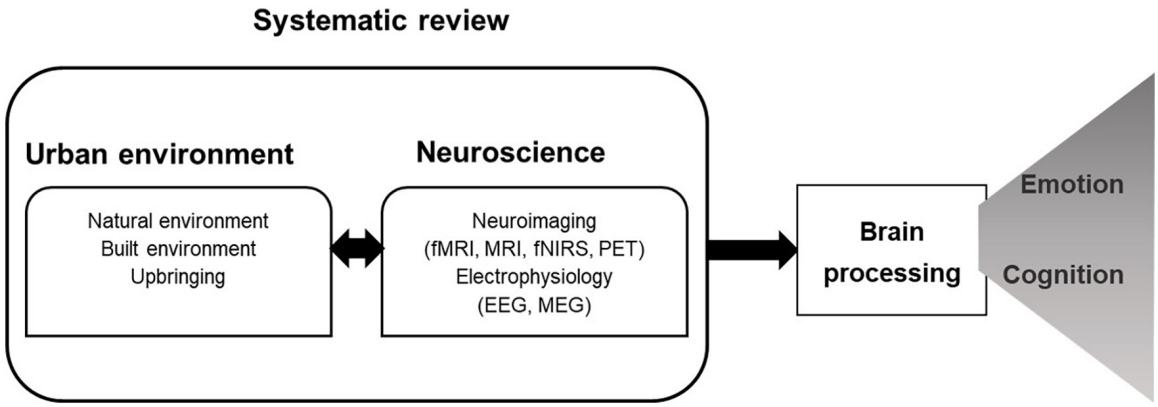

FIGURE 1
Conceptual model guiding the review.

of Science, and Scopus. Search terms were related to both urban built and natural environments, as well as to quantitative research measuring brain activity effects of such exposures (see Table 1).

Study selection and data collection process

Initially, two different teams, with a neuro-scientific/medical (LAA, IA, BM) and urban/architectural (PM, AB) background, screened each paper independently according to titles and abstracts to identify an eligible subset. Then, an independent evaluation of the retained articles was firstly performed by two authors (LAA, IA) and then validated by the last author to ascertain eligibility and scan reference lists. Selected studies were then distributed among three authors (LAA, IA, BM) for a full-text review (see Figure 2), who independently extracted data into a pre-designed data extraction table (including information about the authors, publication date, objectives, study design and setting, population characteristics, sample size, environmental exposures, brain measurements, results summary, and major limitations). Discrepancies were resolved by team discussion. To ensure the screening process was accurate, 5% (169) of 3,380 titles and abstracts were randomly selected and cross validated among the teams to assess data reliability (the internal validation was good with a Kappa score of 78%).

Quality appraisal and synthesis of evidence

We assessed the quality of included studies using a standard quality assessment criterion (40). Two authors independently scored (zero for no, one for partial, two for yes) on fourteen criteria (which address biases in sample selection, quantification of barriers, measure of the outcome, appropriateness of statistical analysis, or adjusting for confounders when applicable). Any disagreement was resolved by discussion. The sum of all scores was then divided by the highest possible score (see Table 2).

In addition to the overall assessment and to facilitate the synthesis of evidence, studies were grouped according to whether they used fMRI, fNIRS, or EEG methodologies (and detailed findings were reviewed by BM and LAA, respectively).

Results

Sixty-two studies (published between 1981 and 2021) were included in the review. More than half of the studies (n = 34) were published in the last three years, suggesting an emerging trend of interest in the topic.

General characteristics of included studies

Regarding the research participants, almost all studies (n = 59) recruited healthy volunteers; and among these, the vast majority (95%) were adults (age ranging from 20 to 41). Only five studies focused on a more vulnerable population such as the elderly (age ranging from 75 to 83); and a minority of studies (n = 3) targeted clinical (adult) populations, involving patients with anxiety, gambling, or other psychiatric disorders.

To investigate how urban exposure affects the brain, published work focused primarily (95%) on the neural response evoked by certain city living features; and only a few (n = 3) explored a rather long- impact of urban childhood upbringing or urbanicity. In terms of experimental setting, most studies were laboratory-based (66%), but some (n = 18) performed their

TABLE 1 Search terms used for the query.

Urban							AND	Measurements
Strictly urban	OR	Natural			OR	Built		Brain activity
Title/Abstract		Title/Abstract	AND	Title/Abstract		Title/Abstract	AND Title/Abstract	Title/Abstract
urban outdoor urban space* urban environment* urban landscape* urban design urban planning urbanism urbanization urbanization urban form urban morphology urban infrastructure urban typology urban typologies urban renewal city space city environment city landscape city design city planning city form cities public space urban public space urban centre urban inner circle historical centre city centre interior city urban expansion urban dynamic urban footprint urban life urban artifacts Urban nature		park fest tree garden natural environment* natural infrastructure* natural space* natural landscape* natural outdoor* nature-based nature exposure nature contacts nature sound natural environment* natural setting* green space* greenspace* greenery blue space* bluespace*		urban* city cities		Street neighbourhood neighbourhood building built environment physical environment	urban* city cities	EEG Event related potential ERP magnetic resonance imaging MR MRI fMRI neuroimaging time resolved spectroscopy Near-infrared spectroscopy NIR NIRS Positron Emission Tomography PET MEG

experiments in an outdoor or real-life setting. It is interesting to also note that in certain cases (n = 5) the experiments contemplated an "hybrid" design–i.e., the protocol included both an indoor and an outdoor session (for the urban exposure and/or for the outcome brain evaluation).

When investigating the city living exposure, almost two-thirds of the studies compared natural-either green (parks, forest, or gardens) or blue spaces (lakes or riverbanks), against built environments (including highly busy areas or quieter neighborhoods). Fifteen studies performed comparisons just between natural environments and only four focused on different built environments.

For assessing brain activity, more than half of the included studies (n = 37) used EEG outcome measures; moreover, fMRI (n = 14) or fNIRS (n = 11) were also commonly used. It is also important to note that the vast majority (81%) of included studies (i.e., directly measuring brain activity), further complemented their analysis with other evaluations–including self-reported psychological assessments (including, for example, stress, and perceived restorativeness scales) or other physiological signals (heart rate, blood pressure, galvanic skin response, and cortisol levels).

Functional magnetic resonance studies

Most studies using fMRI aimed to understand the relationship between the responses in certain brain areas and the exposure to either urban built or natural environments. The presentation of such findings will be followed by the studies addressing the consequences of urban upbringing and/or city living on cognitive-emotional brain processing.

Functional magnetic resonance-based studies comparing urban built and natural exposure

Kim et al. (41) compared the brain activity while participants were exposed to pictures of natural landscapes (including natural parks, forests, and mountains; but not necessarily from a city environment) against urban scenes (with prominent built infrastructures, such as tall buildings). It was found that frontal (particularly in the superior and middle frontal gyrus), parietal (in the superior parietal gyrus), precuneus and anterior cingulate cortex regions were the ones more active for the natural setting (also perceived by the participants as the condition eliciting more comfort). On the other hand, urban scenery (with greater suffocating and accustomed self-ratings) elicited more activity in temporal regions (anterior temporal pole, hippocampus, and parahippocampal gyrus), occipital cortex (predominantly the middle occipital gyrus) and amygdala. A second study from the same group (42) and using similar rural and urban images found, not only similar regional activation patterns, but also observed a predominant activity in

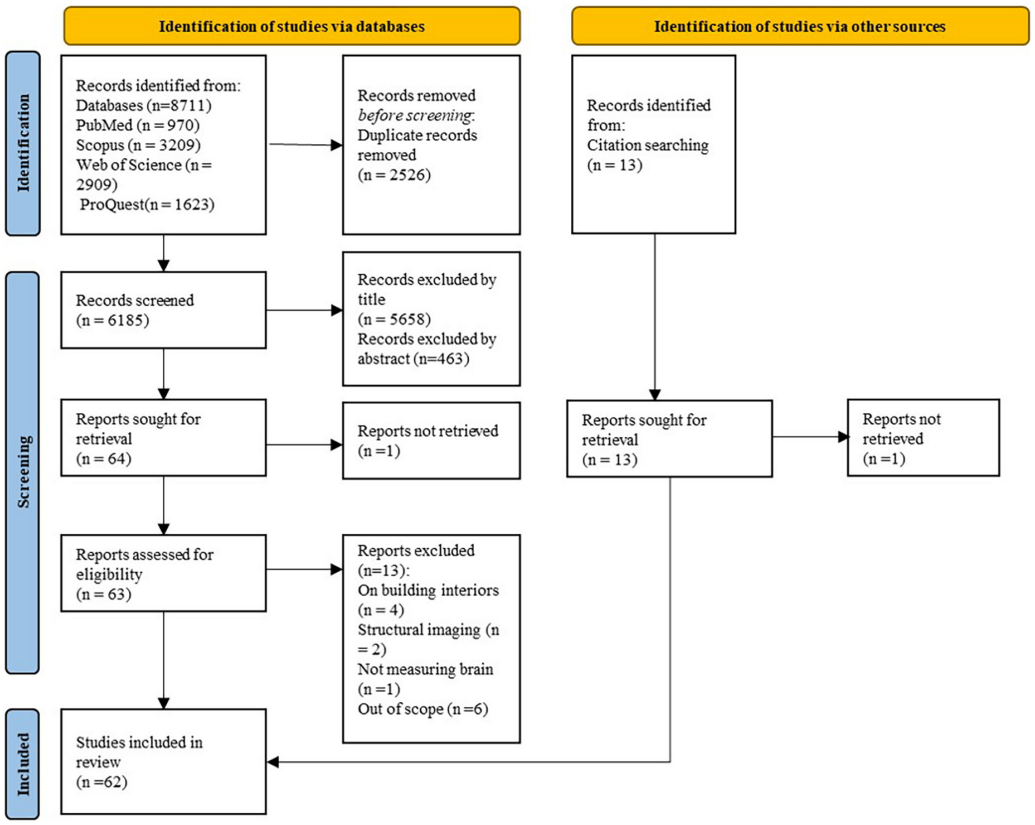

FIGURE 2
Preferred reporting items for systematic reviews and meta analyses (PRISMA) flow diagram of the selection process.

the basal ganglia–very much involved in motivational, reward and hedonic value coding, for the rural scene condition.

Rather focusing on a comparison within a particular cultural context, Seiyama et al. (43) used two kinds of landscape pictures in Japan–traditional architecture/nature (JTANs) and modern cityscapes (MCs) images. After the fMRI experiments, subjects were asked to rate the emotional valence of all trials. A negative correlation was observed between JTAN self-reporting and the right precuneus activation–suggesting that this region might be more involved in the underlying process of objective scenes evaluation than the emotional experience. Another interesting observation was the fact that viewing pleasant pictures elicited greater activation of dorsal visual pathway regions (such as the superior parietal lobule and medial occipital gyrus); whereas unpleasant landscapes predominantly activated the ventral visual pathway (including the inferior temporal and inferior frontal gyri), as well as the cerebellum. It is therefore possible that, when evaluating the pleasant landscape scenery, a higher spatial processing (e.g., location and depth)–linked to the dorsal pathway–got more prominence than the ventral visual object recognition computation (e.g., color and shape).

Neural correlates of restorative environments–either built or natural–were investigated by Martínez-Soto et al. (44), by showing to participants in the fMRI photographs considered to have a high and low restorative potential. Despite not observing significant differences in the perceived stress ratings before and after viewing both types of images, some brain regions were differently activated. Specifically, the high restorative group lead to responses in the left middle frontal gyrus, insula, and cuneus. Furthermore, in the low restorative potential group, there was a higher posterior cingulate activity, which is usually associated with endogenous attention (45). Kunh and colleagues (46) adopted a complementary approach not only by focusing on the functional connectivity between brain areas (instead of task-related regional activation) but also by matching the presented natural and built environmental images according to the dimension of perceived pleasantness (although the images used were not necessarily from an urban context). They found higher levels of connectivity when participants were watching natural scenes (compared to images with buildings), making this network activation less pronounced if the individuals' upbringing was longer in major cities.

In line with the potential role of urban green space exposure in buffering against the development of mental illness, Bratman et al. (47) investigated whether a 90-min nature walk (versus an urban walk) decreased rumination–a maladaptive

TABLE 2 Data extraction and quality assessment.

References	Author	Type of participant	Sample size	Age mean, SD	Measure	Environmental features	Setting	Quality score
[41]	Kim GW et al. 2010	Volunteer	28	26.9, 1.2	fMRI	Built and Natural environment	Indoor	0.91
[42]	Kim TH et al. 2010	Volunteer	30	27,3.7	fMRI	Built and Natural environment	Indoor	0.91
[43]	Seiyama et al. 2018	Volunteer	11	23.4,1.2	fMRI	Built and Natural environment	Indoor	0.86
[44]	Martínez-Soto 2013	Volunteer	28	36.18,12.46	fMRI	Built and Natural environment	Indoor	0.73
[46]	Kuhn et al. 2021	Volunteer	24	28.5, 9.5	fMRI	Built and Natural environment	Indoor	0.95
[47]	Bratman et al. 2015	Volunteer	38	26.7	fMRI	Built and Natural environment	Indoor	0.91
[48]	Tang et al. 2017	Volunteer	31	25	fMRI	Built and Natural environment	Indoor	0.86
[49]	Zhang et al. 2019	Volunteer	16	20.5,1.71	fMRI	Natural environment	Indoor	0.86
[50]	Chang et al. 2021	Volunteer	44	23.7	fMRI	Built and Natural environment	Indoor	0.91
[51]	Tost et al 2019	Volunteer	33	23.64,2.42	fMRI	Natural environment	Hybrid	0.86
[52]	Heller 2020	Volunteer	122	23,3.4	fMRI	Built and Natural environment	Hybrid	0.91
[17]	Lederbogen et al. 2011	Volunteer	55	N/A	fMRI	N/A	Indoor	0.77
[56]	Reed et al. 2020	Volunteer	487	31.9,8.9	fMRI	N/A	Indoor	0.82
[57]	Lemmers-Jansen et al. 2020	Clinical	69	21.5,2.9	fMRI	N/A	Indoor	0.86
[58]	Yamashita et al. 2021	Volunteer	25	23, 1.67	NIRS	Built and Natural environment	Indoor	0.91
[59]	Song et al. 2018	Volunteer	17	21.1	NIRS	Built and Natural environment	Indoor	0.77
[60]	Lee 2017	Volunteer	18	26.7,0.7	NIRS	Built and Natural environment	Indoor	0.82
[61]	Jo et al 2019	Volunteer	29	22.3,2.1	NIRS	Built and Natural environment	Indoor	0.95
[62]	Ochiai et al. 2020	Clinical	12	36.9,11.5	NIRS	Built and Natural environment	Indoor	0.68
[63]	Yu et al. 2017	Volunteer	7	36.3,11.3	NIRS	Built and Natural environment	Indoor	0.77
[64]	Zhang et al. 2020	Volunteer	31	22.6, 1.4	NIRS	Natural environment	Indoor	0.91
[65]	Park et al. 2007	Volunteer	12	22.8,1.4	TRS	Built and Natural environment	Indoor	0.77
[66]	Joung et al. 2015	Volunteer	8	22,2.2	NIRS	Built and Natural environment	Outdoor	0.82
[67]	Song et al. 2020	Volunteer	29	21,1.4	NIRS	Built and Natural environment	Outdoor	0.86
[68]	Horiuchi et al. 2014	Volunteer	15	36	NIRS	Natural environment	Outdoor	0.86
[69]	Ulrich 1981	Volunteer	18	23	EEG	Built and Natural environment	Indoor	0.77
[70]	Elsadek et al. 2021	Elderly	34	82.9, 0.78	EEG	Built and Natural environment	Indoor	0.68
[71]	Olszewska-Guizzo et al. 2018	Volunteer	29	31,10.3	EEG	Built and Natural environment	Indoor	0.86
[72]	Jiang et al. 2019	Volunteer	50	22,1.65	EEG	Built and Natural environment	Indoor	0.73
[73]	Roe et al. 2013	Volunteer	20	30	EEG	Built and Natural environment	Indoor	0.73
[74]	Gao et al. 2019	Volunteer	116	20.7,2.13	EEG	Built and Natural environment (VR)	Indoor	0.95
[75]	Mahamane et al. 2020	Volunteer	74	23	EEG	Built and Natural environment	Indoor	0.82
[77]	Grassini et al. 2019	Volunteer	32	24.7,3.7	EEG	Built and Natural environment	Indoor	0.91
[78]	Kim et al. 2019	Volunteer	60	31	EEG	Built and Natural environment	Indoor	0.91

(Continued)

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TABLE 2 (Continued)

References	Author	Type of participant	Sample size	Age mean, SD	Measure	Environmental features	Setting	Quality score
[79]	Elsadek et al. 2021	Elderly	34	82.9, 0.78	EEG	Built and Natural environment	Indoor	0.68
[80]	Bailey et al. 2018	Volunteer	10	20	EEG	Built and Natural environment	Hybrid	0.68
[81]	Olszewska-Guizzo et al. 2021	Volunteer	25	40,17.8	EEG	Built and Natural environment	Indoor	0.91
[82]	Chiang et al. 2017	Volunteer	180	21.4,1.81	EEG	Natural environment	Indoor	0.82
[83]	Wang et al. 2020	Volunteer	180	20.7,2.56	EEG	Natural environment	Indoor	0.68
[84]	Chang et al. 2007	Volunteer	110	Not mentioned	EEG	Natural environment (VR)	Indoor	0.82
[85]	Olszewska-Guizzo 2018	Volunteer	32	27,6.5	EEG	Natural environment	Indoor	0.86
[86]	Wang TC et al. 2020	Clinical	77	59.7	EEG	Natural environment	Indoor	0.68
[87]	Rounds et al. 2020	Volunteer	29	27.65,10.04	EEG	Built environment	Indoor	0.86
[88]	Hu et al. 2020	Volunteer	8	18.41,1.28	EEG	Built environment	Indoor	0.68
[89]	Deng et al. 2019	Volunteer	60	20.8,1.02	EEG	Natural environment	Outdoor	0.77
[92]	Herman et al. 2021	Volunteer	17	NA	EEG	Natural environment	Outdoor	0.64
[93]	Lin et al. 2019	Volunteer	240	20.2,1.76	EEG	Natural environment	Outdoor	0.95
[95]	Lin et al. 2020	Volunteer	40	20.5,1.87	EEG	Natural environment	Hybrid	0.77
[96]	Yi et al. 2021	Elderly	59	75,5	EEG	Natural environment	Outdoor	0.95
[98]	Karandinou & Turner 2018	Volunteer	10	Not mentioned	EEG	Built environment	Outdoor	0.45
[101]	Hollander et al. 2016	Volunteer	5	Not mentioned	EEG	Built environment	Outdoor	0.41
[103]	Aspinall et al. 2013	Volunteer	12	30	EEG	Built and Natural environment	Outdoor	0.59
[104]	Al-barak et al. 2017	Volunteer	10	21	EEG	Built and Natural environment	Outdoor	0.73
[105]	Hassan et al. 2018	Volunteer	60	20,1.42	EEG	Built and Natural environment	Outdoor	0.91
[106]	Chen et al. 2016	Volunteer	32	20.6,1.6	EEG	Built and Natural environment	Outdoor	0.86
[107]	Reeves et al. 2019	Volunteer	36	41,11 M	EEG	Built and Natural environment	Hybrid	0.82
[108]	Olszewska-Guizzo et al. 2020	Volunteer	22	32.9,12.7	EEG	Built and Natural environment	Outdoor	0.86
[110]	Hopman et al. 2020	Volunteer	29	25,6.76	EEG	Natural environment	Outdoor	0.91
[112]	Elsadek et al. 2019	Volunteer	25	23.5,1.5	EEG	Built and Natural environment	Outdoor	0.95
[113]	Tilley et al. 2017	Elderly	8	75.75,6.76	EEG	Built and Natural environment	Outdoor	0.5
[114]	Neale et al. 2017	Elderly	95	76,8.15	EEG	Built and Natural environment	Outdoor	0.82
[116]	Neale et al. 2020	Elderly	95	76.55,8.15	EEG	Built and Natural environment	Outdoor	0.95

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pattern of self-referential (most often negative) thought very often linked to depression. To further complement reports of the healthy participants, the authors also evaluated the fMRI activation in the sub-genual prefrontal cortex (sgPFC)–a brain region known to be particularly active during sadness, behavioral withdrawal, and negative self-reflective processes. In fact, a walk in the natural setting significantly reduced the neural activity in sgPFC (and independently of the walk-related physiological activations).

Functional magnetic resonance-based studies focused predominantly on exposure to natural environments

In addition to the comparative built versus natural approach, some authors focused their analysis on the qualitative properties of the natural environments. For example, Tang et al. (48) compared the restorative value of exposing healthy volunteers to four different types of landscapes images: urban, mountain, forest, and water (to note, though, that the authors did not balance the order of exposition, being the urban exposure always the first experimental condition). Results from self-report questionnaires revealed significant restorative benefits with all natural environments–with the most value being for the water and mountain scenarios, and the least for the urban images. However, fMRI analyses only showed greater activation of the cuneus when urban scenes were compared against either mountain or water landscapes. Moreover, for the latter condition there was also a significant activation of the right cingulate gyrus and the left precuneus. In another example, Zhang and colleagues (49) tried to explore whether the appreciation of images from natural landscapes differed from the artificiality of human-built gardens (controlling for aesthetic pleasantness, familiarity, and color preference). Despite some common patterns of brain response–involving the medial orbitofrontal cortex and the precuneus, the authors report activation preferences for gardens in the middle temporal gyri and middle cingulate cortex; whereas, the greater responses for natural landscapes were found in the Rolandic operculum and in the anterior cingulate cortex. Finally, the contrast between gardens and natural scenes elicited stronger activation in the inferior occipital gyrus, hippocampus, cuneus, superior parietal lobule, and supplementary motor area.

The other important question is whether brain activation matches the parametric changes in the quantity of green-space exposure (including trees, bushes, and grass). Chang et al. (50) not only aimed to clarify this, but they also tried to relate such neural activation to stress and preference-related reports. By showing participants a variety of images from various metropolitan areas (equated for luminance and chrominance) with different levels of green space density, they elicited significant activations (above and beyond lower order features) in both ventral posterior cingulate cortex (vPCC) and cuneus. Furthermore, through an effective connectivity analysis they show that vPCC has a feedforward influence on cuneus, as well as on other spatial and attentional brain regions (including the superior parietal lobule and the middle frontal gyrus). The systematic dose-dependent changes elicited in brain activity (which was paralleled by changes in stress-ratings) raise awareness for the therapeutic potential for natural environmental exposure.

Finally, there has been a more recent wave of studies that adopt a mixed-methods approach that combine epidemiological, psychological, geographic information system (GIS), and neuroimaging tools (51, 52). Such innovative work uses a hybrid approach that links real-life data collection with fMRI brain activation in laboratory-based paradigms. Tost et al. (51) aimed to unravel some to the biological underpinnings on how real-life urban green space (UGS) exposure improves human well-being. First, in a group of healthy young adults living in the city of Manheim (Germany), they found a significant within-subject positive correlation between emotional well-being (assessed with a smartphone-based electronic diary) and the GIS-quantified UGS exposure during seven consecutive days. Then, they asked participants to perform a well-known emotion-related fMRI paradigm. Interestingly, individuals with the greatest positive impact of UGS exposure on the "real-life" ambulatory emotional ratings, were the ones showing lower activation on higher-order emotion regulatory brain regions–including the dorsolateral and the dorsomedial pre-frontal cortex. In another good example, Heller et al. (52) explored the potential of geolocation tracking, experience sampling and fMRI to examine whether daily variability of physical location (i.e., the number of unique locations visited in each time) was associated to self-reported positive affect. They not only found such positive location-affect relationship, but they also observed that this effect was stronger for those individuals who exhibited a stronger functional connectivity between the ventral striatum and hippocampus–two regions, respectively related to reward (53) and novelty processing (54). These findings suggest that the environmental diversity could be a key element to provide positive affect in everyday life and ultimately a sustainability strategy for the individual well-being.

Functional magnetic resonance-based studies related to urban upbringing and current city-living

Urban living has been associated with an increased risk of mental health disorders and chronic physical illness, being stress a potential key mediator factor (55). In a ground-breaking study, Lederbogen and colleagues (17) used fMRI to assess whether urban upbringing and city living could impact the human brain mechanisms that regulate social stress. Participants were distributed in three groups according to whether they

were living in a city (>100.000 inhabitants), a town (>10.000 inhabitants) or a rural area. Moreover, how much they spent their childhood in a city was also considered. Brain activity and its link to social stress regulation was investigated using the Montreal Imaging Stressed Task (MIST)–a well-known social stress paradigm (where participants do arithmetic tasks under time pressure and that elicits neural, cardiovascular and hormonal stress-related responses). Significant differences for the level of current city living were found in the amygdala, which increased stepwise from rural to small towns, and being the highest for city dwellers. Meanwhile, urban upbringing was rather associated with the activity in peri-genual anterior cingulate cortex (also increasing linearly with the highest activation for participants raised entirely in the city environment; and lowest for those brought up in rural areas).

Another relevant study (56) focused their work on the potential relationship between upbringing, urbanicity and the human reward-based system–more specifically to dopamine gene variations. Genetic data was collected from three independent groups and included information about catechol-O-methyltransferase, dopamine receptors D1 and D2. Both gene-related data and childhood urbanicity levels were considered as independent variables for the analysis of fMRI activation during a N-back working memory task. The results showed not only independent main effects of both variables on the middle frontal gyrus activity, but they also revealed that urban childhood upbringing interacted with each gene pattern to affect cerebral responses. Being the dopamine system and the reward circuitry so much involved in neuropsychiatric illnesses, this work suggests a genotype-phenotype pathway by which neural effects of upbringing exposure could be linked to adulthood disorders.

To further explore the links between urban upbringing, its related social stress effects and psychiatric illness, Lemmers-Jansen et al. (57) investigated the association between urbanicity and trust in both healthy and psychotic individuals. They employed a trust game paradigm, which is based on investment and repayment from another player and involving two scenarios–cooperative and unfair situations. Participants were divided in two upbringing groups, categorized as high urban (>2,500 inhabitants per km^2) and low urban (<2,500 inhabitants per km^2) upbringing places. They found an interaction effect linking urbanicity and cooperative condition to the amygdala activation. Higher-urban patients showed a stronger left amygdala reduction of activation than lower-urban patients during cooperative investment; and this was more pronounced in psychotic patients (than in healthy controls). Therefore, their results potentially suggest that low-urban upbringing could be a protective factor for cooperation, which then increases trust related to positive feedback, and this is reflected on amygdala activation.

Functional near-infrared spectroscopy studies

Indoor functional near-infrared spectroscopy-based studies comparing urban built and natural exposure

Like the approach used in several fMRI studies described above, indoor fNIRS work also compared the neural activation to urban built and natural exposure (with images or videos). In a study by Yamashita et al. (58), healthy volunteers viewed different types of nature and built environments for 3 min while fNIRS was performed. Viewing images of nature, not only increased self-reporting of comfort and relaxation, but it also reduced the activity in the right orbitofrontal cortex–a region associated with affective processing and control. Similar pre-frontal fNIRS activation was observed in experiments using only images of specific types of natural settings, including forest landscape with metasequoia tree (versus imagery of buildings in Tokyo) (59) and visual landscapes of traditional gardens (versus images of a commercial area in Korea) (60).

Other studies considered either different stimuli or group of participants. For example, when healthy volunteers (61) and patients with gambling disorder (62) listened to forest sounds (in contrast to city noise) or watched garden video clips (compared to urban scenes) (63), their pre-frontal fNIRS response was also reduced.

Finally, a randomized controlled study examined whether greenery pictures or brief relaxation techniques (and compared to a control task where subjects stared at a fixation cross) would affect brain responses during an arithmetic task (64). Contrary to the authors' expectations, a significant activation of frontopolar and (left) orbitofrontal cortices was found only after the brief relaxation practice; and not after viewing greenery pictures or the control task.

Functional near-infrared spectroscopy-based studies performed outdoor

A major advantage of fNIRS compared to fMRI is the portability, and some studies performed their measurements in a real-world scenario (65, 66). For example, Park et al. (65) tested fNIRS activation before and after a 20-min walk in a forest or a built space. The results for the forest walk corroborated the reduced activation in pre-frontal areas.

To refine the protocol of the above mentioned study involving a walk in either a forest or in the city, Joung and colleagues (66) used a similar methodology but positioned participants (for 15 min) on the rooftop of a building (to avoid some stress related to the feeling of being watched in the street by other people). Other groups also aimed to compare the fNIRS activity viewing scenery in a forest area (67); whereas others contrasted the neural responses of participants when seated in a real forest with the curtain of their tent opened, as opposed to a closed-curtain condition (68). In any case, and across the

different settings, the exposure to nature induced a reduced pre-frontal fNIRS activation.

Electroencephalography studies

The number of EEG studies conducted in the laboratory were similar to those running the data collection in an outdoor setting. Moving out of a controlled environment into a more ecological setting allows more naturalistic data collection, but at a cost of increased movement artifacts or reduced signal quality of wearable EEG devices (not to mention, the presence of other covariates sometimes difficult to control). We start by presenting the findings of laboratory-based studies, where most of the analysis focused on more conventional EEG type of analysis. Then, we will describe the EEG studies obtained in outdoor settings. Importantly, most of the latter studies used commercial devices with either a very limited number of electrodes or with manufacturer's algorithms relating EEG evaluation directly to some emotional or brain states. The lack of knowledge about the raw EEG signals in such studies impacts on the validity of their results and on their interpretation.

Indoor electroencephalography-based studies comparing urban built and natural exposure

Most indoor EEG studies compared brain activity while participants viewed images of either a natural or a built environment. An old EEG spectral analysis study (with only two bipolar pairs of electrodes) was one of the first to evaluate the neurophysiology underlying the exposure to different types of landscape scenes (69). It was found that imagery of different natural environments–with water and vegetation–elicited higher mean alpha values than built environment photographs. Moreover, the alpha activity was lower for blue space scenes than for greenery vegetation ones–likely due to attention-holding properties of water views.

More recently, a study that randomly assigned participants to two different offices–one with a window opened onto a green area and another one with a window looking out onto an urban built space–similarly observed an increase in frontal and occipital alpha waves for the nature exposure scenario (70). Also exploring the view from windows but using rather photographs taken at different heights (and considering various amounts of built space and vegetation), Olszewska-Guizzo and colleagues (71) found similar greater (right-side) frontal alpha power for the highest amount of green-space–but only at a certain height of view (12th floor compared to 3rd, 6th, and 24th floors). Both studies relate the alpha activity in the brain with its association with states of alertness–higher alpha activity has been linked to lower levels of arousal and feelings of relaxation.

In another study, Jiang et al. (72) broaden not only the spectrum of EEG analysis (recording beta, delta, theta and gamma frequencies also with a 2-electrode device), but also the experimental conditions–by considering pictures of gardens, natural scenery landscape, forest, city landscape and an urban city traffic (the latter was considered the reference condition). In all frequency bands, participants presented higher values for landscape pictures than the reference condition. In a cluster analysis, Roe et al. (73) conducted a similar experiment but using a 12-channel device and a commercial software for performance metrics (that considers also spectral decompositions). It was found that exposure to "green" landscapes photographs generated greater levels of "meditation" and lower "excitement", as opposed to urban built scenes. Interestingly, no significant differences were found among relatively similar environmental scenarios presented through VR devices–although the EEG device used for this study had a very limited electrode count (74).

Adopting an event-related EEG approach with a 14-channel device, Mahamane et al. (75) compared the brain activity on a passive oddball viewing task using scenic images of natural and built environments. Their focus was on the elicited P3 and late positive potential (LPP) responses–neural correlates of categorical differences (greater activation for rare stimuli or updating contexts) and stimulus valence/pleasantness (negative stimuli have greater positive amplitude), respectively. Despite failing to see significant effects for the P3 component, built environments elicited a significantly greater LPP activity than natural environments–supporting the views that the latter context leads to better perceived pleasantness (76). With a similar goal but using a more sophisticated methodological design and equipment, Grassini et al. (77) found that urban scenery (when compared to different types of natural scenery–such as desert, forest, snow, and water) elicited a temporally complex signal: with sustained early posterior negativity, usually associated with increased visual attentional processing; followed by an increased P3 component, potentially reflecting some higher allocation of resources or cognitive load; and finally a minor LPP-like component, differently from what was previously described. To note that for this study, urban images with faces of people or other semantic content (letters or numbers) were excluded, to avoid potential attentional bias.

Considering that the presence of people in a landscape (either built or natural) modulates the human interaction with its surroundings–particularly perceived fear at night, Kim and colleagues (78) compared the alpha and beta frequencies (with a 14-channel EEG) when subjects are exposed to images with or without people on both urban (or "grey") or nature-dominant (or "green") environments. More important than the higher mean alpha values elicited for the "green" conditions (like the one reported by others), a significant "Landscape type" × "Human presence" interaction effect was observed. Hence, this study highlights that the presence of people is relevant when interpreting any comparative studies about built versus natural environments.

Demographic characteristics of the participants or specific contexts could also be relevant when interpreting the potential effects on the brain of more built or natural environments. A study with an elderly population exposed to a very particular type of "green"–a forest landscape showing bamboo grove (79), confirmed the previously described increased alpha waves for natural environments observed in young adults. One must be aware when interpreting this finding that the latter bamboo landscape had some sort of semantic meaning to the cultural background of the participants (being a symbol of virtue in certain oriental communities). One study (80) related the brain activity on a 5-channel wireless EEG to cognitive testing–following a 30-min walk either in a natural outdoor environment or inside a recreational building space. The study revealed significantly increased theta waves in the frontal cortex and stronger alpha levels in occipital regions–also considered a more "meditative state"–for the outdoor sessions; and the findings of "meditation" and "relaxation" (i.e., increased alpha power across all electrodes) lasted longer after walking in nature.

Related to the recent societal challenge of COVID-pandemic, Olszewska-Guizzo et al. (81) questioned whether the exposure to natural environments during the lockdown measures could mitigate the impact on mental wellbeing and on EEG frontal alpha asymmetry (FAA)–a brain pattern that is commonly associated with positive approach/emotions. Participants also viewed videos of different types of built and natural urban public spaces before and after the pandemic. Contrary to the expected, high nature exposure during the lockdown was associated with significantly lower FAA scores (i.e., less positive emotional response), potentially because individuals who did not go out much had a more approach-related motivation for the outdoor videos. Moreover, the FAA decreased the most for the videos of residential green areas–despite containing natural elements and being technically considered a green space. The authors highlighted the importance of exploring the quality of green spaces as well as of the nature experiences in the city.

Indoor electroencephalography-based studies focused predominantly on exposure to natural environments

Several studies focused solely on the different features of natural landscapes and their brain effects. For example, Chiang et al. (82) investigated how participants' exposure to photographs of nature with a variety of locations and vegetation density modulated the alpha frequency (on a 2-channel EEG headset). Greater alpha activity was observed for interior forest photos (i.e., enclosure constituting of surrounding trees and other types of vegetation), as compared to the other two settings–where patches were visually overlapped or possible to be seen from far away. No significant differences were revealed across the different vegetation densities. The authors interpreted the findings by considering that a more unified vegetation arrangement could elicit mental relaxation (as opposed to a multi-level structure). Using a similar low-density EEG device and a set of videos reproducing bamboo forests with different characteristics, one study (83) found that values for high/low beta and alpha waves decreased relatively fast after the videos started and then remained stable. Moreover, the decrease was greater for bamboo forests with a higher canopy density (i.e., the proportion of area covered by the crown of bamboo trees) and a lower tilt ratio (i.e., the ratio of the number of bamboos with an inclination angle offset from vertical greater than 45°).

Inspired by the ideas of ART (32), Chang et al. (84) explored the neurophysiological response (with a multi-modality 8-channel EEG system) using images reproducing natural restorative environments (images selected by the authors for each of the known restorativeness components: being away, extent, fascination, and compatibility). All natural-restorative environments elicited greater mean alpha values in both hemispheres, when compared against a non-viewing (or control) condition. Another study (85), also exploring similar theoretical assumptions, intended to examine the effects of 3D fixed-angle videos representing natural landscapes (rated by experts as contemplative)–i.e., green outdoor settings having long vistas, lush seemingly-wild vegetation, the presence of symbolic elements, and smooth landforms, and non-contemplative ones on brain activation patterns. They surprisingly did not find effects on alpha power (and its asymmetry) but observed greater beta power on the right temporal lobe for contemplative stimuli–which was interpreted by the authors as either a potential reflection of a more holistic perception of such natural landscapes; or a consequence of a saliency-related attention due to fascination.

In attempt to translate the above-mentioned restorative qualities of natural environments into a therapeutic context, one study randomly assigned patients with generalized anxiety disorder either to virtual natural scenes or to virtual abstract paintings (86). Their EEG alpha activity (recorded with only four channels) was assessed at baseline and after some aerobic exercise. In both exposure groups, as compared to the pre-time exercise, participants presented higher alpha levels. In addition, alpha values for the virtual natural scenery were higher–suggesting that the restorative properties of natural environments may potentially help a clinical population.

Indoor electroencephalography-based studies focused predominantly on exposure to built environments

Two indoor studies took advantage of virtual reality (VR) to investigate the effects of different types of built environments. Rounds et al. (87) aimed to understand which architectural features could serve as possible landmarks during urban navigation tasks and used posterior theta band activity as a signature of spatial awareness and memory. Salient buildings (i.e., those with contrasting characteristics

to their surroundings) were found to elicit more of such neurophysiological signatures than non-salient buildings. Moreover, those incorporating twist designs (i.e., designs with a progressively rotated façade as it gains height) benefited from a greater theta activity effect (as well as greater self-reported visual attractiveness). The second study (88) combined immersive VR with a 5-channel EEG device to evaluate the impact of a new light rail line in the suburbs of Washington D. C.–by comparing the pre- and post- VR built projections. While self-reported evaluation about the urban features (such as the building types or height, or street characteristics) revealed a clear preference in favor of the new scenario, neurophysiological activity was harder to interpret. Rather than analyzing the raw signals, the collected brain data was categorized into six emotional states with the help of a commercial software–being this a strong reason for the findings' limitations.

Electroencephalography-based studies performed outdoor

Several cases of outdoor EEG studies were performed in a real-life or more ecological contexts. Deng et al. (89), for example, explored the restorative effects of exposure to three different types of natural landscape–water, lawn, and mountain. They have also looked at various landscape elements and components of a traditional urban park. It was found that the mountain landscape showed the highest alpha mean values in the frontal region–considered by the authors as consequence of a good balance between openness and enclosure, leading to a sense of encirclement and privacy positive for relaxation (90). Such findings support other indoor research emphasizing that certain types of landscape promote health in vulnerable groups (such as elderly people) (91).

Besides some benefits associated to certain type of environmental typologies, it has been debated whether the quality of the urban green space could disparately affect individual brain responses. To address this, Herman et al. (92) compared passive recreation in informal green spaces (i.e., patches of vegetated areas scattered throughout the city which are not included in the city's planning documents as green spaces, but provide numerous benefits to residents, including walking paths and pet areas, recreational spaces, urban agriculture lots) against traditional urban green spaces (e.g., city parks recognized or planned for recreational use by inhabitants)–in terms of well-being perception and portable EEG activity. No significant differences were observed–for frontal alpha, beta, delta, gamma, or theta oscillations–between the two exposure types. However, while comparing such green areas as a function of the different levels of human interference (e.g., paths and presence of urban furniture), the levels of alertness–reduced alpha and enhanced theta–increased for the wilder scenarios.

The human presence has also been investigated in real outdoor settings as a possible relevant factor for the behavioral dynamics of city dwellers. Lin et al. (93), conducted an experiment where participants could either walk or sit in small urban green spaces with different per capita area (i.e., with high, middle, and low population density). The results showed that in general, participants had a greater frontal beta/alpha ratio for sitting (versus walking) in such green areas–interpreted as a proxy for being more nervous and stressed (94). However, this latter effect was also modulated by the number of people surrounding the individual; being walking in a highly populated and sitting in isolation the conditions with better neurophysiological signatures. A similar experiment was performed (95), where two groups were assigned to either a walking or sitting group, which performed a high-pressure learning task and then recovered in a simulated green space. Once again, results showed that walking groups had lower beta/alpha ratio (also with more self-reports of positive valence and meditation-like experience) as compared to the sitting group. On the other hand, the latter profited from higher "focus" values, suggesting that sitting may contribute to some sort of attentional restoration. It is worth mentioning that both studies were conducted in very small areas delimited by a more unified vegetation–prompting the question of whether participants would experience even a greater effect in a richer natural landscape.

The impact of physical activity in urban green spaces has also been studied in more ecological settings. Yi et al. (96) investigated how two different "forest therapy" programs–active walking versus a resting control group–could impact elderly individuals. The results showed that active walking had an increase in alpha and beta values (from baseline). Considering that some literature suggests that alpha wave activity and beta wave power decrease in early stages of Alzheimer's disease (97), this was interpreted by the authors as a potentially relevant finding for cognitive decline prevention.

Two studies focused on how the brain reacts to navigational tasks and specific architectural features within the urban built environment. Karandinou and colleagues (98) have recorded neurophysiological data while participants navigated between specific buildings in Portsmouth city center. Beta activity peaks were observed in critical way-finding choice points in a way that has been also seen by others (99, 100); although beta activity reduced if the places were more familiar to the subjects. The other interesting study conducted by Hollander et al. (101), tested the concept of "Cognitive Architecture" (CA), meant as "a set of principles for architecture and planning practice" (102). In their experiment they contrasted two walking sessions in the Boston city area–one in a historical ethnic neighborhood with mixed-use buildings and the other one in a reconstructed area with less architectural character. The five participants in the experiment revealed greater levels of "attentiveness" and "meditation" EEG measures while being in the historical neighborhood, than for the reconstructed one. Noteworthy, besides the use of a proprietary algorithm labeling

the EEG signal into such brain states (with no access to raw data findings), results were also not statistically robust given the small sample size.

Only three outdoor studies compared the impact of free walks in the built versus natural environments. Both works by Aspinall et al. (103) and Al-Barrak et al. (104) examined, using an EEG proprietary algorithm, brain responses when subjects walked through urban green spaces versus other city areas. The first study (103) explored the urban emotional experience through three different areas in Edinburgh: a shopping street, a green space street and a busy commercial district. Participants showed less "engagement" (i.e., directed attention), "frustration", together with an increase in "meditation", when passing from the shopping area to the urban green space. Conversely, when moving from the green area to the commercial district the levels of "engagement" raised (although this effect size was relatively small). The second study (104) rather focused on participants moving across a cafe, a supermarket and a garden; reporting stronger "meditation" levels for the garden as compared to the supermarket. Finally, Hassan et al. (105) investigated the physiological relaxation effects of a 15-min bamboo forest walk versus a similar walk in the city. Participants showed greater frontal alpha activity when walking in the bamboo forest (and compared to the city walk), an observation that is in line with other studies where walking in green areas induced a mental state of relaxation (93, 95).

A somehow different approach was used by five other studies, which decided to seat participants in different real-world scenarios and evaluated the associated brain activity. Chen et al. (106) compared EEG recordings while in a garden versus a highway island with traffic; and more efficient and strong connectivity was found during the exposure to the natural setting. Similarly, Reeves et al. (107) compared (using an indoor space as the control condition) a natural wetland area against a traffic scene. A stronger beta activity was seen for the green area–leading the authors to suggest that an involuntary attentional shift may take part of the "fascination" process; and something also supported by Olszewska-Guizzo et al. (85). However, the authors acknowledged a substantial deterioration in the EEG signal quality (due to movement artifacts and possible electrode displacement) that could undermine the robustness of the results. In another study (108), participants were either exposed to a busy street, an urban park or a green neighborhood, and the comparison was focused on the frontal alpha asymmetry (FAA)–which is positively related to favorable emotions and negatively associated to depression (109). After adjusting for environmental conditions, higher FAA values were observed in the urban park compared to the street; an observation that suggests a possible like between nature exposure and positive mood. On the other hand, Hopman and colleagues (110) investigated the changes in averaged resting state posterior alpha power (PA)–associated with an increased external processing (111)–before, during, and after a multiday exposure to nature (which included the possibility of hiking) or to urban built environments. Participants showed lower PA while exposed to the natural condition than to the urban built. Additionally, the effects of green façades were compared as possible sources of mental relaxation by Elsadek et al. (112). Here, authors found a significant increase in alpha waves for the frontal and occipital regions when participants were exposed to a façade with climbing plants as opposed to a white wall.

Finally, three of the outdoor studies deserve particular attention as they targeted their experiments for an elderly population. Tilley et al. (113) showed, with a mixed methods approach, that participants had EEG signals compatible with a reduced attentional effort (using an algorithm and not the raw signal data) while walking in a green space versus an urban busy (and with more built environment) street. Furthermore, the level of frustration did not appear to change while transitioning from the green to the busy environment. In a relatively similar design but adding also a "quiet" urban area, Neale and colleagues (114) instead observed an increased level of "engagement" in green areas as compared to both busy commercial and quiet residential areas. In their analysis they also found evidence supporting that part of this effects could be related to a greater attentional demand from the poorest quality of paving in natural settings (this observation is particularly interesting and worth exploring given the walking vulnerability of elderly people). Alternatively, it is also possible that the drive is rather a stronger bottom-up processing linked to involuntary attentional mechanisms (115). In a repeated experiment (116) but using the actual raw EEG data, the same group observed an attentional shift neural signature- that is lower beta activity (117)–for the green setting. On the other hand, no differences in alpha activities were observed among the urban busy with green environment–despite an increase in busy urban environments as compared to the urban quiet ones. One possible explanation could be derived by the subjects' familiarity with places, causing a more relaxed state as opposed to the less familiar quiet areas.

Discussion

Most analyzed studies have provided a wealth of neuroscientific evidence corroborating the often-found individual self-reports–as well as prominent environmental psychology assumptions–that nature exposure and biodiversity (over heavily dense built spaces) promote positive health and well-being benefits. Our discussion aims to resume and integrate the findings, by promoting a novel neurourbanistic perspective relevant for mental or public health practitioners and policymakers involved in urban planning and design.

The urban built environment (such as buildings, city traffic scenarios, etc.) is commonly regarded as more demanding from a cognitive perspective (when compared to natural landscape). In our analysis, non-natural city-built artifacts, likely due to

a more complex architectural geometry or optical dynamics, were found to engage brain areas and elicit evoked responses associated with greater cognitive (e.g., perception and attention) demand and negative emotional states. More specifically, the urban built stimuli elicited greater fMRI activation in brain areas involved in higher-order visual processing–such as the middle and inferior occipital gyri; in episodic/semantic memory, spatial navigation and object recognition–including hippocampus, parahippocampal gyrus, and anterior temporal lobe; and in both fear and stress-related responses–the amygdala. These findings provide neural substrates to the ART concept of directed attention fatigue (more linked to higher order mental functions) and, thus, support that a more complex urban built environment could provide fewer capacities to recover and restore (32).

On the other hand, exposure to nature elicited brain activation in areas more related to basic visual processing (cuneus), visuospatial perception (superior parietal gyrus), sensorial integration (insula), emotional or cognitive control (including the anterior cingulate cortex and the precuneus) and motivational behavior (basal ganglia). Such cognitive functions are more linked to simpler or "bottom-up" attentional processes of alerting and orienting, and demand relatively few mental resources. Hence, these neural correlates suggest that the interaction with natural settings, as suggested by the ART, are compatible with our intrinsic motivations and provide restorative opportunities. Interestingly, such nature-evoked activation not only seems to have a positive dose-related effect (48), but it is also modulated (with more temporal activation) by human intervention in such setting–as in the case for human-built gardens (in comparison to wild nature) (49). To note that the precuneus and the anterior cingulate cortex have also been shown to respond–as for nature–for beauty and pleasantness assessments in other visual contexts (such as paintings) (118, 119). All these observations are in favor of a greater adaptation of the visual system for recognizing natural (and ecologically or more biological elements) images (120)–in line with the "aesthetic advantage" of nature in ART (32) and the biophilia hypothesis (34). Similarly, they also contribute for a better understanding of the potential restorative properties, as well as role in emotional regulation and cognitive control of nature exposure.

The results from EEG and fNIRS corroborated the above-mentioned fMRI observations. Most EEG studies emphasized that exposure to natural settings increased conventional neurophysiological markers of quiet or relaxing wakefulness–such as the increase in alpha rhythm. Similarly, fNIRS-pre-frontal responses, often associated with mental effort or cognitive demanding states (121), were also consistently diminished in several natural settings (in contrast to the hyperactivity seen when the exposure was for urban built space). The advantages of temporal resolution and portability of EEG and fNIRS techniques allowed them to provide complementary evidence. In fact, not only different temporally-evoked EEG responses could be observed–consistent with early attentional drive elicited by urban built scenery (77); but also, the findings observed in well-controlled laboratory experiments could be translated to outdoor real-life scenarios. Interestingly, the effects across the temporal domain have not been particularly considered in most environmental psychology theories (32, 34), although it deserves further attention given the neural findings.

Another important finding that goes beyond the impact of either built or natural surroundings, was the immediate (or more direct) and later (or upbringing) neural modulation observed because of social interaction or population density. The importance of activity-setting and social context within the normative framework of ART theoretical has also been highlighted by some authors (122). Urban density has been associated to anxiety, stress, loss of perceived control and increased risk for mental health (123, 124); but the involved brain mechanisms are unknown. Overcrowding can be felt as a social stressor, inducing feelings of violation of the personal space and activation of amygdala areas linked to fear response and negative affect (125–127). Other results further described activity in other relevant emotional- and stress-related brain areas–including the amygdala, sub-genual, and medial pre-frontal cortex. This was not only seen for comparative works on built versus natural scenarios, but it was also important when looking at the city upbringing effects. Moreover, we found brain research data supporting the epidemiological evidence either arguing for an association between raising children in cities and increased risk for psychiatric illness (56) or demonstrating that green-spaces proximity during infancy promotes mental well-being (128).

Finally, some recent studies also highlighted the expected participation in the human-environmental interaction of brain structures responsible for motivation and reward-based learning–as, for example, the basal ganglia and the orbitofrontal cortex. In addition, environmental enrichment seemed to incentive explorative behavior and self-reported positive affect, which also involves reward processing brain regions (52). This work is particularly interesting as it takes advantages of computational theories on how a learning agent interacts with the environment, at the same time as it opens doors to better links with neuropsychiatric disorders (129).

Limitations

Despite the structured search strategy in multiple databases and the specific eligibility criteria and goals, this review has limitations. First, we tried to specifically focus on the relationship between neuroscience and urban planning/design–instead of architecture and interior design, hence it is possible that some relevant work could have been excluded. Secondly, we did not perform a meta-analysis to obtain greater accuracy or improve effect sizes across the different exposures. Even

if we didn't set any initial time limit in our search criteria, the search did not contemplated studies from last year and only publications in English were considered–which may have resulted in some studies being missed. Moreover, we did not include other important city environmental factors, such as pollution, noise, or temperature. Finally, this review contemplates only studies with direct brain measurements, neglecting that stress, and emotional aspects could also be assessed indirectly by other biometric metrics.

Additionally, the reviewed studies also have limitations. While analyzing the data we have identified gender (more males) and age (preference for the young) imbalance; and few studies focused on clinical populations or had a longitudinal design (limiting causality inference). Another limitation often found was the short exposure time for the tested conditions (for example, for either the natural or built environmental scenarios), as well as the simplicity of the stimuli used–being predominantly images (which do not allow a full experience of the context). In addition, there were little attempts in the indoor studies to combine different sensorial modalities (i.e., most studies used visual stimuli, and a few used sounds), and get closer to a more realistic scenario. Regarding the tools to investigate the brain activity, several outdoor studies using EEG did not follow conventional neurophysiological analytics–but rather used proprietary (and not necessarily validated) algorithms to directly provide an emotional or behavioral outcome. Finally, the impact of potential confounding variables (e.g., noise exposure, social interactions, personality traits, and other context variables) was frequently disregarded.

Future research

While preforming this review, one of our intentions was to raise attention and identify key priorities for future research. First, we consider important to focus more on the underlying processes bridging urban environmental exposure and mental health and well-being. The effects of nature exposure to certain psychiatric diseases have been addressed by some studies, but their physiology is still largely unknown. By contemplating more interventional and longitudinal studies, future research could advance our knowledge and will be a step forward to move from associative to causal conclusions.

Using clinical populations in more studies may also help generating stronger evidence-based recommendations for urban health decision making. Similarly, the aging challenges associated with modern societies also prompt a call for more work on the elderly population and in those within initial stages of dementia. Some architectural features attract visual attention and remain in short term memory (87), which could possibly have some benefits in subjects with spatial disorientation. In fact, the link between urban built or natural exposure, some restorative or meditative effects and neuropsychological performance has been rarely explored. A focus on vulnerable groups (not only the elderly or patients, but also migrants or other minorities) and gender differences and balance should, thus, be further explored.

While analyzing the indoor and outdoor studies, we did not find studies comparing or particularly addressing the limitations and trade-offs of both types of experimental settings. If in the future one wants to take advantage of the emerging wearable neurotechnology, such information is critical. Furthermore, no attempts have been made to obtain multimodal data–by using, for example, EEG-fMRI techniques (or EEG electrical source imaging). This could be an important validation step to allow the field to move with more confidence from lab to the street experimentation.

Despite some recent efforts highlighting the importance of individual variability (or vulnerabilities), more research is needed. We also believe that future studies should incorporate, when interpreting the neural responses, socio-economic factors (e.g., social network or educational background); as well as other individual aspects (such as personality traits or baseline levels of stress or anxiety symptoms). There is a clear need to go beyond the idea that some exposure relates to a positive or negative brain activation (and links to self-reports). And finally, only with a thorough understanding of the human-environment relationship we can better address long-term effects of certain types of childhood upbringing.

Conclusion

The growing urbanization and climate change are major and contemporary global challenges and, among their implications in several other domains of our daily lives, they are recognized as important risk factors for mental health issues. Modern cities are complex and multifaceted entities, which involve infrastructural, social, cultural, economic, and biological aspects. Urban science is now more than ever considered as a *trans*-disciplinary field that aims to integrate novel theoretical ideas and methodological tools for better policy and decision making. Similarly, neuroscience involves many fields of research–from molecular to clinical–and the benefits of its application in real-world settings is becoming increasingly recognized. Despite being in its infancy, neurourbanism is a new field that explores the neurological or other biological underpinnings of mental states and disorders to achieve better and healthier living in urban areas. This review focused on brain research insights from the human-environment interaction to discover ways of fostering and improve the mental health and well-being of city dwellers. We collected and described in detail the wealth of evidence from fMRI, EEG, and fNIRS studies supporting how the urban environment–built or natural–can affect the neural circuits of our brain.

Our findings offer a more integrative view on how the urban built artifacts elicit greater perceptual and cognitive

processing, at the same time as it expands our knowledge about the restorative potential of natural environments. The neural physiology, connectivity, and dynamics described underpins the neural substrates for theoretical constructs in environmental psychology. As a whole, our neuroscientific evidence assists urban planners, organizations, and communities to increase green and blue spaces, considering their biodiversity and quality, within the urban infrastructure–as it potentiates neural mechanisms linked to mental restoration (82) and stress-recovery (49, 108, 112). Furthermore, supporting the access to local natural landscapes (such as wetlands and forests) provide positive cognitive and emotional feedback to both healthy and more vulnerable groups (e.g., the elderly population) (89, 96, 106). Furthermore, city planning should consider overcrowding as a potential stressor (17), and take into account the space behavior in relation to per capita area when designing urban built and natural spaces (93).

Finally, more work is needed to fully embrace the underlying mechanisms linking cities and brains. The future research in the field should take advantage of the impressive modern tools to characterize behavior, neurophysiology, and environmental factors–it is an exciting time for putting neurourbanism in practice!

Author contributions

LAA, PM, and BM defined domains. LAA, IA, and BM conducted a full-text analysis. LAA, DAB-M, and BM performed a quality assessment and analyzed the results. LAA and BM participated in writing the manuscript. LAA, IA, AB, PM, and BM contributed to assessing the relevance of the articles by abstracts and titles and analyzing and extracting data. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Urbanization and depressive symptoms among middle-aged and older adults in China

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Aims: Urbanization plays an important role in individuals' health. However, it is difficult to isolate healthy migrant effect between urbanization and health. This study examined the effects of urbanization on depressive symptoms and its possible pathways among Chinese middle-aged and older adults independent of the influence of health-selective migration.

Methods: Using the baseline survey of the China Health and Retirement Longitudinal Study, this study compared the depressive symptoms among three groups (urbanized rural residents, rural non-migrants and urban non-migrants). The 10-item Center for Epidemiologic Studies Depression Scale (CESD-10) short form was used to measure depressive symptoms. Logistic regression models and Structural Equation Model (SEM) were applied to examine the association between urbanization and depressive symptoms and the corresponding potential mechanisms.

Results: Our final sample contained 11,156 respondents with an average age of 58.91 (SD = 9.48), with 5,142 males (46.09%) and 6,014 females (53.91%). Compared with urbanized rural residents, rural residents were more likely to have depressive symptoms (OR = 1.19, 95% CI = 1.07, 1.32), and urban residents were associated with a decreased risk of depressive symptoms (OR = 0.81, 95% CI: 0.70, 0.94). A large proportion of the association between urbanization and depressive symptoms were mainly mediated by social participation, income and living conditions.

Conclusions: Planned urbanization had an independent impact on decreased depressive symptoms. Improvements in social participation, income and living conditions are the main drivers behind this relationship. Additionally, urbanization compensates for the negative impact of depressive symptoms from disadvantaged early life conditions, but it cannot eliminate the gap between urbanized rural people and urban non-migrants.

KEYWORDS

urbanization, depressive symptoms, mechanism, middle-aged and older adults, the China Health and Retirement Longitudinal Study

1. Introduction

Depression is a major public health concern. According to WHO data, approximately 280 million people suffer from depression. The disease burden of depression ranks 13th among the leading causes of disability-adjusted life years (DALY) (1). It will increase the risk of adverse health outcomes, including cardiovascular diseases, dementia, cognitive impairment and falls (2–4) and cause a huge economic burden (5), with an annual medical cost of $326 billion in the US in 2020 (6) and €118 billion in Europe in 2005 (7). Depressive symptoms are very common among middle-aged and older adults, presenting in up to one-third of older adults (8), and serve as an early indicator of depression (9). In China, the lifetime prevalence of depressive symptoms in adults over 50 years old is ∼4.1% (10), which has hurt health systems (1), with an annual medical expense of RMB 4.4 billion in urban areas (11). In the context of aging in China, where the population aged 65 and over is projected to account for 26.1% by 2050, it is important to study the prevention and intervention of depressive symptoms to improve the quality of life of middle-aged and older adults.

The health effect of urbanization is controversial (12). On the one hand, it provides protective health opportunities, especially for people with depression, such as better living conditions, infrastructure development and access to health care (13–15). On the other hand, it is also associated with a range of factors that can further increase depression risk due to rapid and unplanned urbanization progress, including poor quality of healthcare, economic pressure and environmental hazards (16, 17). In the past decade, China has been rapidly urbanized, with a proportion of 49.68% in 2010 to 63.89% in 2020, far exceeding that of other countries. Different from other low-income and middle-income countries, China's rapid urbanization is mainly encouraged by governments (16, 18). Therefore, this process avoids the negative impact of urbanization, such as slums in developing countries in the progress of urbanization (19), which is partly due to the expansion of housing and infrastructure brought about by urban planning (20). Additionally, due to the improvement of socioeconomic conditions, infrastructures, healthcare services, and social inclusion in urban areas (13, 14), this process may provide benefits to health promotion.

China's urbanization is usually accompanied by large rural-to-urban migration, including voluntary migration and forced urbanization (20). The drivers of voluntary migration can be described as economic, social and environmental push or pull factors such as better job opportunities or housing conditions in urban areas (21). As a result, those migrants are selected individuals who tend to be healthier according to the hypothesis of health-selective migration. Furthermore, according to salmon bias, migrants with poor health status are more likely to return to their destinations (22). For these reasons, it remains unclear whether the health benefits observed in urban areas are due to urbanization or simply the result of health-selective migration. Urbanization in China can also include forced urbanization in urbanized villages, where the whole village territory is converted to urban land, and the so-called forced upstairs farmers are involuntarily relocated from traditional scattered houses to urban multistory housing buildings by the government (23, 24). Therefore, urbanization can be studied as an exogenous variable since these population groups do not experience migration in urbanized villages. In light of the above, planned urbanization in China provides us with a special opportunity to study the causal relationship between urbanization and depressive symptoms. To isolate the effect of health-selective migration or salmon bias, this study identifies a population in China. This population is transformed from local villagers to urban citizens without being influenced by migration, sharing early life experiences with the rural population that has stayed in rural areas all their lives and their later years with urban residents that have resided in cities throughout their lives.

Although previous studies have documented significant associations between urbanization and depression (13, 25), most of these related studies are mainly regional surveys, and few of them detect the underlying mechanism through which urbanization influences depressive symptoms. Additionally, it is difficult to rule out the effect of health-selective migration or salmon bias in much of the research on urbanization and improved health (16, 22). To bridge these gaps, this study aims to investigate the association between urbanization and depressive symptoms and further detect the potential causal pathways between them by using large nationally representative data from the China Health and Retirement Longitudinal Study (CHARLS) among middle-aged and older adults in China. This study may help to understand the impact of urbanization independent of health-selective migration on depressive symptoms and provide references for the early prevention and intervention of mental health promotion for low-income and middle-income countries in their urbanization progress. Based on prior screening and background, we hypothesize two empirical predictions under the hypothesis that urbanization is good for depressive symptoms as follows:

Hypothesis 1. The health of the in urbanized rural residents will be (a) better than that of the rural residents, and (b) worse than that of the urban residents.

Hypothesis 2. (c) More engagement in social participation, (d) more utilization of healthcare, (e) higher individual income, and (f) better living conditions in urban areas will contribute to this advantage.

2. Materials and methods

This study used data from the China Health and Retirement Longitudinal Study (CHARLS), which is a nationally representative survey in China. The objectives of this survey were to provide information about demographic characteristics,

health status and functioning, health care and insurance, and socioeconomic conditions. Face-to-face computer-assisted personal interview (CAPI) was conducted every 2 years. Samples were obtained by the probability-proportional-to-size (PPS) sampling technique to ensure the representativeness of the sample. In the first stage, all counties (except Tibet) were stratified by region, urbanity and GDP per capita. Primary sampling units (PSUs) were chosen among each selected county using administrative villages in rural areas or neighborhoods in urban areas, which comprised resident committees. In each PSU, samples of dwellings were randomly selected using mapping software named CHARLS-GIS. In total, the survey was conducted in 28 provinces, 150 countries or districts, 450 villages or urban communities, consisting of people aged 45 and over living in households, but the baseline respondents who later entered into an institution were followed. The national baseline survey was conducted from May 2011 to March 2012. The total sample households included 23,422 dwellings, and the survey finally managed to contact 17,708 individuals in 10,257 households with an overall response rate of 80.5% (26). Further details of the sample are available elsewhere (26), and data can be accessed through its official website (http://charls.pku.edu.cn/).

According to a prior study (16), we chose the CHARLS baseline survey since it contained more sufficient information on individual migration experience, while migration indicators in surveys of younger cohorts were deduced based on the 2011 survey. From the 2011 wave, we excluded 2,748 participants without information on migration and 1,731 participants without information on depressive symptoms. A total of 1,773 participants who were migrants were excluded, and 310 cases of missing covariates or mediators were also excluded. Our final sample contained 11,156 respondents with an average age of 58.91. Figure 1 presents a flowchart of the 2011 CHARLS study.

2.1. Measures

2.1.1. Depressive symptoms

Our outcome variable was a binary measure (i.e., whether depressive symptoms were present). This study used the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10) short form (27), which has satisfactory validity and reliability among the Chinese older (28) population (28, 29). The respondents were asked to rate their positive feelings, negative emotions and somatic symptoms experienced over the past week through the 10 following questions on a 4-point scale from rarely or none of the time (<1 day) to most or all of the time (5–7 days): (1) I was bothered by things that do not usually bother me; (2) I had trouble keeping my mind on what I was doing; (3) I felt depressed; (4) I felt everything I did was an effort; (5) I felt hopeful about the future; (6) I felt fearful; (7) My sleep was restless; (8) I was happy; (9) I felt lonely; (10) I could not get "going". The depressive symptoms index was obtained from the sum of the scores of the 10 questions ranging from 0 to 30, and a higher score indicated higher depression. According to previous studies, a cutoff point of 10 was of good validity among older Chinese respondents (27, 28); consequently, respondents who scored at least 10 in this study were considered to have depressive symptoms.

2.1.2. Residential status

Our independent variable was categorized as urbanized rural residents, rural non-migrants and urban non-migrants. We used both the migration information and official household registration system information (called Hukou in Chinese) to measure residential status. In detail, we first removed migrants from the sample and took non-migrants as the targeted study population to study the exogenous effect of urbanization on depressive symptoms. To do this, we used data on their birthplace, current place of residence, age at migration and duration of migration to measure their experience of migration, excluding return migrants (having a migration experience of more than 6 months outside their birthplaces) and early-life migrants (the age at migration is younger than 16). We then used Hukou status to classify the non-migrant population into three groups: (1) urbanized rural residents, referring to local urbanized residents who have realized urbanization in their towns and villages and used to hold rural Hukou when relating to the birthplace. Their lives began in the countryside, while their later lives are in the city; (2) rural non-migrants, referring to people who live in rural areas and hold rural Hukou; (3) urban non-migrants, referring to people who are born and live in urban areas and hold urban Hukou.

2.1.3. Mediators

According to previous studies (13, 14, 20, 30–32), we considered social participation, healthcare utilization, income per capita and living conditions as mediators (see Figure 2).

2.1.3.1. Social participation

In this study, social participation was a continuous variable with an aggregated count (0–11). Respondents were asked about whether they had taken part in any of the following types of social activities in the past month: (1) interacted with friends; (2) played mahjong, chess, cards or went to community clubs; (3) provided assistance to family members, friends or neighbors who do not live together for free; (4) went to a sport, social or other clubs; (5) took part in a community-related organization; (6) engaged in voluntary or charity work; (7) took care of a sick or disabled adult who does not live with the respondent for free; (8) attended an educational or training course; (9) invested in stock; (10) used the internet; (11) other, or (12) none of these. We then summed the total number of social activities one participated in from the above multiple-choice question, and the

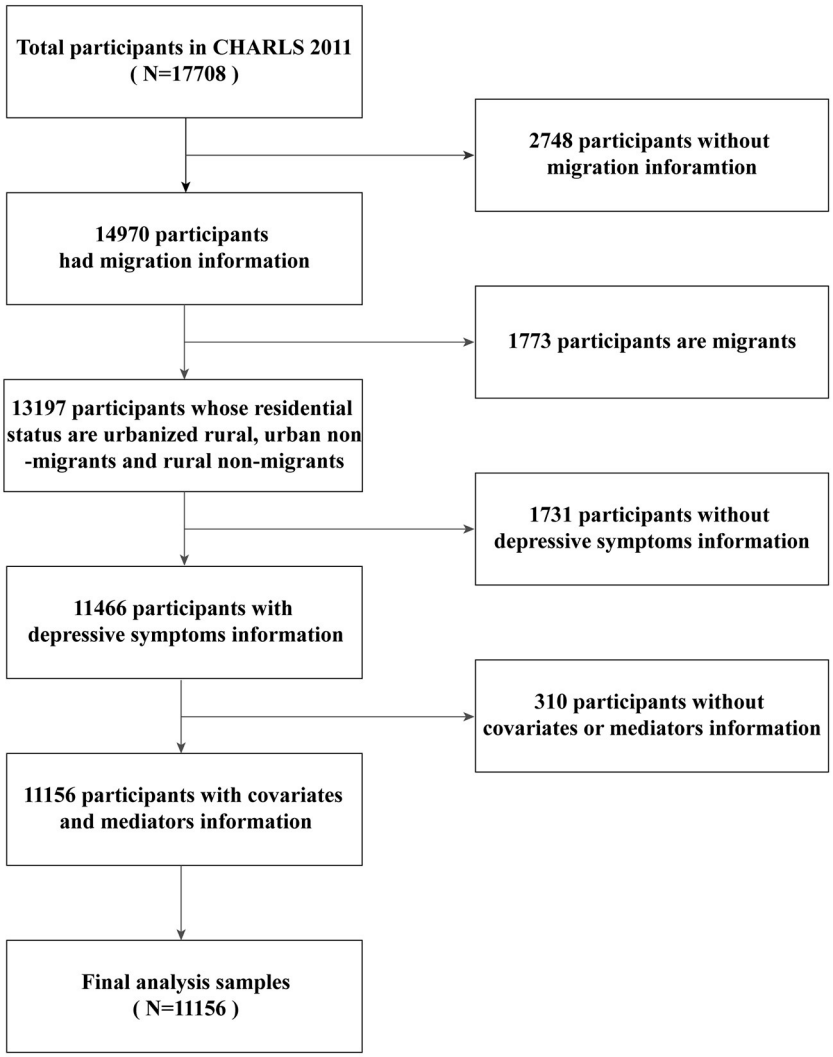

FIGURE 1
Flowchart of sampling of this study.

index ranged from 0 to 11, with higher scores indicating greater social participation.

2.1.3.2. Healthcare utilization

This study generated a binary healthcare utilization variable (1 = yes; 0 = no). In general, healthcare utilization includes outpatient and inpatient care. In this study, we used self-reported information on whether respondents had "visited a public hospital, private hospital, public health center, clinic, or health worker's or doctor's practice, or been visited by a health worker or doctor for outpatient care in the last month" or "received inpatient care in the past year". Based on the characteristics of the data, this study generated a healthcare utilization variable conditioned upon the occurrence of outpatient visits or inpatient visits.

2.1.3.3. The income per capita

The income per capita is a continuous variable. We used the self-reported household income per capita in this study to measure the economic conditions of individuals.

2.1.3.4. Living conditions

Living conditions is a continuous variable measured as an aggregated count (0–7) of seven dichotomous indicators: (1) concrete and steel/bricks and wood, (2) flushable toilet, (3) running water, (4) shower or bath facilities, (5) coal or natural gas supply, (6) telephone connection, and (7) broadband internet connection. The summed score of these seven items ranged from 0 to 7, with higher scores indicating better living conditions.

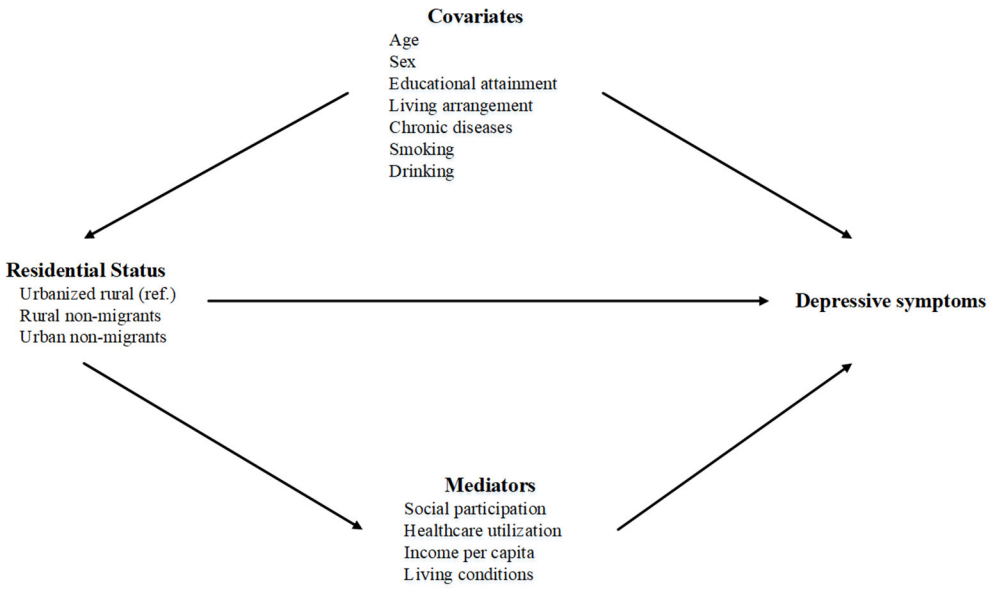

FIGURE 2
Directed acyclic graph (DAG) of the mediation model.

2.1.4. Covariates

We included age (continuous variable), sex (female/male), educational attainment (primary school and below/junior high school and above), living arrangement (living without spouse/living with spouse), chronic diseases (1 = yes, 0 = no), smoking (1 = yes, 0 = no) and drinking (1 = yes, 0 = no).

2.2. Analytic strategy

In this study, descriptive statistics were used to present the characteristics of participants and the prevalence of depressive symptoms in the three groups. To address hypotheses 1(a) and 1(b), logistic regression models were used to examine the relationship between urbanization and depressive symptoms in Models 1, 2, 3, 4, and 5. In Model 1, we controlled all covariates (age, sex, educational attainment, living arrangement, chronic diseases, smoking, and drinking) to examine the joint results. In addition to the factors of Model 1, four mediators (social participation, healthcare utilization, income per capita, and living conditions) were included in Models 2–5 in turn. The analyses were performed with Stata/SE 15.0 for Windows (Stata Corp, College Station, TX, USA). In addition, to explore how social participation, healthcare utilization, income, and living conditions might mediate the association between urbanization and depressive symptoms, we applied the Structural Equation Modeling (SEM) approach to further investigate the association and address hypothesis 2(c), 2(d), 2(e), and 2(f). SEM analyses were conducted using MPlus version 8.3 (Muthén & Muthén, Los Angeles, CA, USA). A CFI > 0.90 was considered an adequate model fit (33, 34), and a p-value of <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of participants

Among the total participants, the mean age was 58.91 years old (SD = 9.48), with 5,142 males (46.09%) and 6,014 females (53.91%). Nearly 4,262 people (38.20%) were measured as having depressive symptoms. Compared with the urbanized rural group, we found that the proportion of depressive symptoms was higher in the rural group. This rural group was older, less educated, fewer living with their spouse, and had higher prevalence of smoking or drinking but fewer chronic diseases. Rural residents were less engaged in social participation, with more healthcare utilization, lower income, and worse living conditions. Relative to urbanized rural residents, a smaller population among the urban group had depressive symptoms. The urban group participants were suffering from more chronic diseases even with younger age, better education level, and living arrangement, and less smoking and drinking. They had better living conditions, more participation in social activities, higher income, and less healthcare utilization. More details of the participants' characteristics are shown in Table 1.

The SEM on depressive symptoms showed an adequate model fit: CFI = 0.930, and the unstandardized estimates appear

TABLE 1 Characteristics of participants ($N = 11,156$).

Characteristics	Urbanized-rural ($N = 2,274$)	Rural non-migrants ($N = 7,135$)	Urban non-migrants ($N = 1,747$)
Depressive symptoms, *n* (%)	776 (34.12)	3,032 (42.49)	454 (25.99)
Age, mean (SD)	58.32 (9.63)	59.33 (9.50)	57.95 (9.09)
Female, *n* (%)	1,271 (55.89)	3,774 (52.89)	969 (55.47)
Primary school and below, *n* (%)	1,624 (71.42)	5,453 (76.43)	641 (36.69)
Living without spouse, *n* (%)	367 (16.14)	1,243 (17.42)	262 (15.00)
Chronic disease, *n* (%)	750 (32.98)	2,317 (32.47)	701 (40.13)
Smoking, *n* (%)	853 (37.51)	2,837 (39.76)	575 (32.91)
Drinking, *n* (%)	878 (38.61)	2,826 (39.61)	656 (37.55)
Social participation, mean (SD)	0.51 (0.87)	0.50 (0.77)	0.67 (1.17)
Healthcare utilization, *n* (%)	556 (24.45)	1,856 (26.01%)	381 (21.81)
The income per capita, mean (SD)	10,628 (29,504)	6,093 (18,533)	26,590 (54,315)
Living conditions, mean (SD)	2.80 (1.44)	2.00 (1.25)	3.76 (1.56)

in Figure 3. Compared with urbanized rural residents, rural residents were associated with an increased risk of depressive symptoms (0.036, $P < 0.002$). It also predicted a lower level of income per capita (−4.533, $P < 0.000$) and worse living conditions (−0.789, $P < 0.000$), all of which were associated with an increased risk of depressive symptoms. Relative to urbanized rural residents, urban residents were not directly associated with depressive symptoms. Urban residents predicted higher engagement in social participation (0.156, $P < 0.000$), less healthcare utilization (−0.026, $P < 0.047$), higher income per capita (15.963, $P < 0.000$), and better living conditions (0.959, $P < 0.000$), all of which were negatively associated with depressive symptoms except healthcare utilization. The direct and indirect effects of urbanization on depressive symptoms are reported in Table 3. Rural residents had both direct and indirect effects on depressive symptoms, but we observed no direct effects in the urban group.

3.2. Logistic regression of the association between residential status and the risk of depressive symptoms

Table 2 shows the results of the multivariate logistic regression analysis between residential status and depressive symptoms. According to Model 1, compared with the urbanized-rural group, the rural group was more likely to have depressive symptoms (OR = 1.42, 95% CI: 1.28, 1.57). The value of OR changed slightly after including the factors of social participation and healthcare utilization in Model 2 and Model 3. After adjusting for income per capita in Model 4, the OR decreased from 1.42 (95% CI = 1.28, 1.57) to 1.38 (95% CI = 1.25, 1.53), and after adjusting for living conditions in Model 5, the odds ratio changed from 1.38 (95% CI = 1.25, 1.53) to 1.19 (95% CI = 1.07, 1.32). Relative to the urbanized-rural group, the urban group was associated with a decreased risk of depressive symptoms (OR = 0.79, 95% CI: 0.68, 0.92) when adjusting for all covariates in Model 1, and the association remained after controlling for social participation (OR = 0.80, 95% CI: 0.69, 0.93) in Model 2 and healthcare utilization in Model 3 (OR = 0.81, 95% CI: 0.70, 0.94). We found that after controlling for income per capita (Model 4) and living conditions (Model 5), this association was not statistically significant, which indicated that this difference may be explained by income and living conditions.

3.3. Pathways between residential status and depressive symptoms

The SEM on depressive symptoms showed an adequate model fit: CFI = 0.930, and the unstandardized estimates appear in Figure 3. Compared with urbanized rural residents, rural residents were associated with an increased risk of depressive symptoms (0.036, $P < 0.002$). It also predicted a lower level of income per capita (−4.533, $P < 0.000$) and worse living conditions (−0.789, $P < 0.000$), all of which were associated with an increased risk of depressive symptoms. Relative to urbanized rural residents, urban residents were not directly associated with depressive symptoms. Urban residents predicted higher engagement in social participation (0.156, $P < 0.000$), less healthcare utilization (−0.026, $P < 0.047$), higher income per capita (15.963, $P < 0.000$), and better living conditions (0.959, $P < 0.000$), all of which were negatively associated with depressive symptoms except healthcare utilization. The direct and indirect effects of urbanization on depressive symptoms are reported in Table 3. Rural residents had both direct and indirect effects on depressive symptoms, but we observed no direct effects in the urban group.

4. Discussion

Using large nationally representative and population-based data, this study was the first to explore the potential mechanism of urbanization and depressive symptoms independent of health selective migration among Chinese middle-aged and older adults. Overall, we found that urbanization was significantly

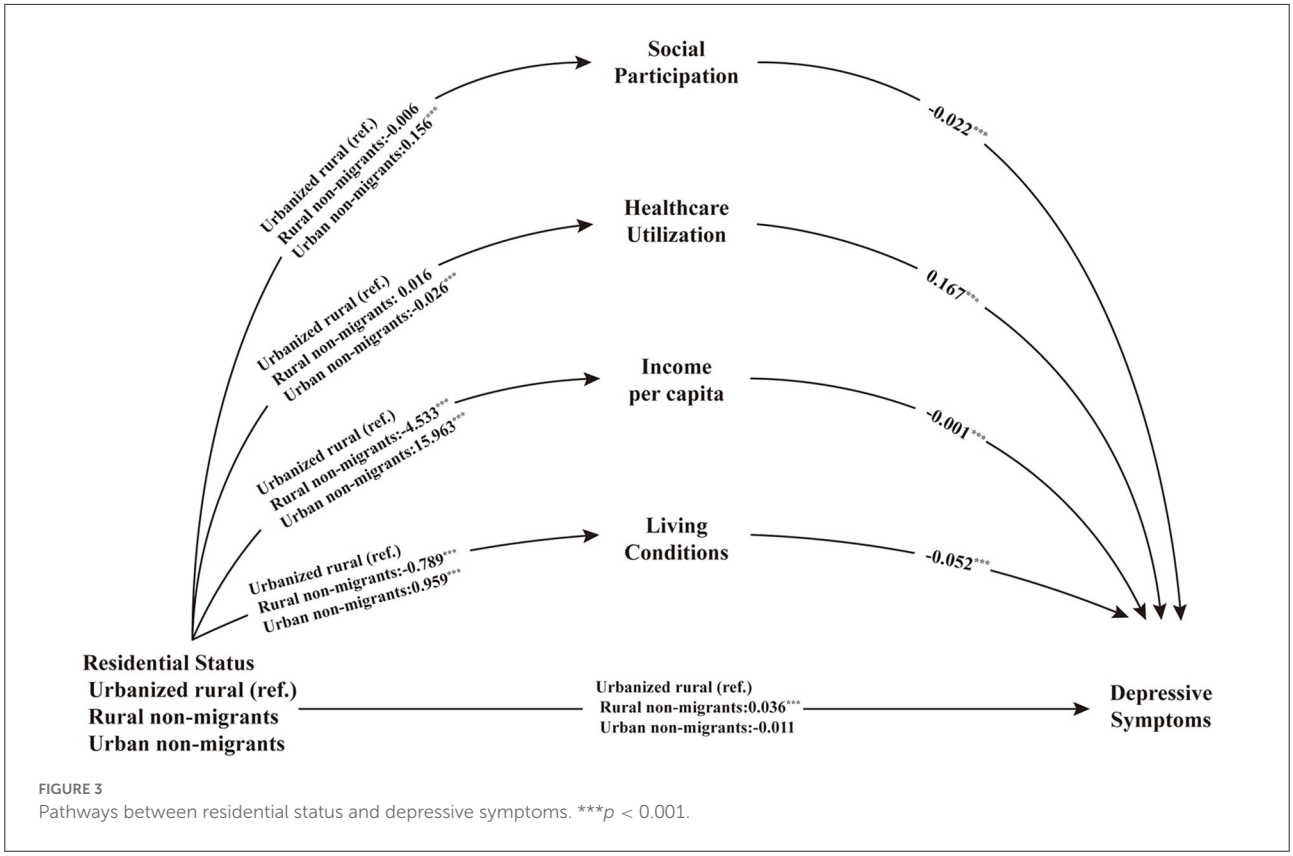

FIGURE 3
Pathways between residential status and depressive symptoms. ***$p < 0.001$.

TABLE 2 Logistic regressions of the association between residential status and the risk of depressive symptoms ($N = 11,156$).

Characteristics	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)	Model 3[c] OR (95% CI)	Model 4[d] OR (95% CI)	Model 5[e] OR (95% CI)
Residential status	–	–	–	–	–
Urbanized rural	Reference	Reference	Reference	Reference	Reference
Rural non-migrants	1.42 (1.28, 1.57)	1.42 (1.28, 1.57)	1.42 (1.28, 1.57)	1.38 (1.25, 1.53)	1.19 (1.07, 1.32)
Urban non-migrants	0.79 (0.68, 0.92)	0.80 (0.69, 0.93)	0.81 (0.70, 0.94)	0.88 (0.76, 1.02)	1.01 (0.87, 1.18)

[a]Model 1 adjusted for residential status, age, sex, educational attainment, living arrangement, chronic diseases, smoking, and drinking.
[b]In addition to factors in model 1, model 2 was adjusted for social participation.
[c]In addition to factors in models 1 and 2, model 3 was adjusted for healthcare utilization.
[d]In addition to factors in models 1, 2, and 3, model 4 was adjusted for income per capita.
[e]Fully adjusted model 5 comprised the factors in models 1, 2, 3, and 4 plus living conditions.

associated with a decreased risk of depressive symptoms. These associations were more likely to be mediated indirectly through social participation, income per capita and living conditions.

Evidence supports that the association between urbanization and depressive symptoms is controversial because of different progress in urbanization and differences in culture, economic development, and environmental factors. On the one hand, the fact of this finding is contrary to the common belief that most people believe individuals living in the countryside are less prone to depression (13), which could be explained by several reasons. In most high-income countries, compared with urban areas, rural residents who haven't experienced urbanization are exposed to less economic stress or environmental hazards (16, 17) and the violent crime rate is lower (35), resulting in a lower risk of depression. In low-income countries, compared to urban residents, rural residents are disadvantaged in socioeconomic status and access to health services, especially mental health services (12). Moreover, urbanization increases the prevalence of depression in most low-income countries, as in the context of India, where unplanned urbanization progresses with the growth of squatters, slum settlements, and apparent poor living conditions (19). On the other hand, previous studies in the context of the United States, where urbanization has orderly coordinated population, land, and socioeconomic subsystems,

TABLE 3 Direct effect, indirect and total effect of residential status on depressive symptoms ($N = 11,156$).

Characteristics	Depressive symptoms		
	Direct effects	Indirect effects	Total effects
Urbanized rural	Reference	Reference	Reference
Rural non-migrants	0.036*** (0.014, 0.058)	0.048*** (0.041, 0.055)	0.084*** (0.061, 0.105)
Urban non-migrants	−0.011 (−0.040, 0.018)	−0.071*** (−0.081, −0.060)	−0.081*** (−0.110, −0.053)

***P < 0.001.

can substantially lower rates of depression with better urban physical and socioeconomic environments (32). Consistent with findings in the United States, our findings also found a beneficial effect of planned urbanization on mental health promotion. Our results showed that the urban group was associated with a decreased risk of depressive symptoms compared with the urbanized rural group, which supported the life course theory, indicating that the accumulation of adverse events in the life course may result in poor health in old age (36). Unlike other countries, China's rapid urbanization has been largely encouraged by the government which helps to avoid the negative effects of urbanization (16, 18). Furthermore, urbanized rural residents might be advantaged in socioeconomic conditions, mental health services and social connection with a lower rate of violent crime due to the expansion of housing and infrastructure which are beneficial for older adults.

Moreover, we found that although urbanization could compensate for the negative impact of depression from disadvantaged early life conditions, it could not completely reverse the health differentials in early life and eliminate the gap between urbanized rural residents and urban residents. Two different hypotheses related to the modifiable or unmodifiable health consequences of adverse events have been proposed. From the embedding mechanism perspective, many diseases developed later in later life originate through epigenetic marks, post-translational modifications, and tissue remodeling caused by adverse events in early life (37), indicating that exposure to adverse events is not modifiable by subsequent wellbeing and that early life is a key period for interventions to reduce future health disadvantages. Another hypothesis suggests that the association of early adversities with health outcomes in later life may be explained by chains of risk (38), which indicates that urbanization may compensate for the negative impact of disadvantaged early life conditions on depression.

Concerning the association between urbanization and depressive symptoms, the primary mediators were social participation, income and living conditions. First, as the urban scaling theory suggests, city environments and urbanization can naturally provide greater social stimulation and connections (32), and engagement in more social participation might improve physical function (39) and cognitive function (40), which is positively related to lower depressive symptoms. This evidence supports our findings that urbanization may create expanding opportunities for social participation, which helps to decrease the risk of depressive symptoms. Second, urbanization may lower the risk of depressive symptoms through the improvement of income level, which is in line with previous evidence (41). As one of the most important indicators of socioeconomic status, income is strongly associated with depression among middle-aged and older adults in China (31, 42, 43). Third, better living conditions may be related to high-quality houses (44) with improved infrastructure and indoor facilities (30), which may be more suitable for middle-aged and older adults to live in and help lower their risk of depressive symptoms. These results may suggest that the mediating effect is a consequence of a planned urbanization process, associated infrastructure improvement, and better social connections.

4.1. Limitations

This study used a large nationally representative sample and isolated the impact of urbanization on depressive symptoms independent of health-selective migration or salmon bias by identifying a population in China who were transformed from local villagers to urban citizens without being influenced by migration. Another key strength of this study is the detection of the mediating mechanisms by which urbanization influenced depressive symptoms. However, this study also had several limitations. First, due to limited data, the measurement of some variables may result in bias in the results when exploring the possible underlying mechanism. For example, outpatient services might be underestimated because some participants may have had no outpatient visits before the survey. Moreover, not including other variables related to depression might have resulted in residual confounding that could bias estimates (45). Second, this study could not rule out a survival effect since healthier people tend to live longer, so we may have underestimated the differences in health conditions, such as depressive symptoms and chronic diseases. Third, limited by data acquisition, urban factors negatively related to health were not included, such as air pollution. Therefore, further studies are needed to confirm the results. Fourth, this survey is a cross

sectional study and it measured the depressive symptoms by self-reported data, which may lead to recall bias (10).

4.2. Conclusions

To conclude, our study found that urbanization in China, almost effectively managed by the state, had an independent impact on decreased depressive symptoms among middle-aged and older adults after isolating the effect of health selective migration. Improvements in underlying mechanisms, including living conditions, social participation, and income per capita, are likely to be the main drivers that benefit mental health among middle-aged and older populations. Additionally, our comparison of depressive symptoms across urbanized rural residents and urban residents who shared similar later urban lives while having different early life circumstances revealed that early adverse events might have the potential to be modified by prevention through socioeconomic factors in later life but might not be fully modifiable. Our findings indicated that planned urbanization may benefit health and wellbeing, and a human-oriented urbanization pattern with orderly industrial upgrading, employment transfer, and population agglomeration may provide support for building a healthy society.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: http://charls.pku.edu.cn/.

Ethics statement

The studies involving human participants were reviewed and approved by the Biomedical Ethics Review Committee of Peking University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

YLu conceived and designed the study. CH and YLu did the initial analysis and supervised data analysis. CH wrote the first draft of the paper. YLu, XX, and XN critically revised the first draft. JL, DQ, YY, and YLi did a thorough language check through the manuscript. CH, XX, JL, XN, DQ, YY, YLi, and YLu reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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How does housing tenure mix affect residents' mental health through a social environment lens? An empirical examination from Guangzhou (China)

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This study demonstrates the mechanisms of housing tenure mix affecting residents' mental health *via* intervening community social environment within public housing practices in urban China. Using a purposive sampling data of six representative public housing estates, we used structural equation models to examine total, direct, and indirect effects of housing mix status on mental health, highlighting the intermediatory roles of social environment variables. On the whole, we find no significant impact of housing tenure mix on mental health; however, housing tenure mix thwarted mental health in a direct way but contributed to it through the mediation of social participation. Regarding the neighborhood effects, we unfold the behavioral, psychological, and socially interactional mechanisms for affecting mental health, by highlighting the direct health implications of social capital, and the mediation of sense of community and social control between social capital and mental health. Finally, we suggest to consider social effects on health grounds into mixed housing strategies in future.

KEYWORDS

income mix, social capital, sense of community, social control, mental health

1. Introduction

For low-income and the housing of disadvantaged populations, public housing initiative is a widely-used political intervention for ensuring and extending their right to develop healthier communities (1). While public housing is often regarded as a cause of poverty concentration and social segregation, leading to negative neighborhood effects on population health (2, 3). Theses contextual effects on public health have been documented and addressed in numerous studies (4, 5), where socialization process has been proposed as an ecological mechanism that mediate between neighborhood characteristics and individual outcomes (3, 6). To combat the undesirable social

issues rooted in public housing, policymakers are keen to increase residential mix of advantaged and disadvantaged groups. Accordingly, mixed housing strategies have become widely advocated and used by politicians to achieve a social mix of population at neighborhood level in the U.S., western European countries, and Australia (2, 7). However, policymakers have not pay enough attention to how different social groups interact as neighbors and how the mixture status of a neighborhood influence individual outcomes. Although housing mix (type or tenure mix) and social mix are theoretically interrelated and have positive effects on people's lives, whether mixed housing strategies can inevitably lead to social mix and overcome negative neighborhood effects has been a subject of debate for a long time (2, 8). Particularly, there is still no clear idea as to how health issues could be addressed through mixed housing strategies within the context of western Europe (i.e., United Kingdom) (9).

The connotations associated with, and initiatives behind, mixed housing initiatives in China are distinct from their counterparts in Western countries. With the progress of housing commodification and marketization in China, mixed housing initiatives has been introduced into public housing documents since 2006, with the its initial aim being to counter housing inequalities and potential social crises (10). Driven by ambitious politically objective of providing a large number of public housing units during a short period since 2008 (i.e., 36 million, 2011–2015), housing mix policy has been operated as a tool to stimulate public housing production to control housing prices. In this sense, mixed housing strategies in China emphasize the mixture of housing tenure, implemented by developers by embedding public housing units into their commodity housing projects. Mixed housing strategies thus become an extension of economic promotion initiatives (11), and its primary objective of tackling housing and social inequities transform into an impetus for local economic growth (12). Thus, mixed housing initiatives have been accused of assuming the role of economic driver rather than social stabilizer in post-reform China (13). Within this context, the neighborhood effects of these strategies on individual health outcomes are even less noticed in political practice. Therefore, this study intended to probe the links between housing tenure mix and social mix, and their effects on social environments and the resultant influence on residents' health outcomes. Two explicit questions are addressed: (1) what is the influence of housing tenure mix on social mix and how does it structure a community's social environment? (2) How do the housing tenure mix/social mix and their resultant socialization process affect individual mental health? This study could contribute to existing literature by its exploration of the mechanisms underlying mental health implications of housing tenure mix in urban China through a social environment lens, putting forward suggestions on embedding health concerns into public housing agendas.

2. Theoretical background and hypotheses

2.1. Social effects of mixed housing strategies

Housing mix and social mix are two interrelated terms in extant research about housing and health. Mixed housing strategies are usually implemented as context-specific tools to reconfigure neighborhood characteristics, and their indirect effects related to housing tenure (i.e. wealth impacts, neighborhood effects) on health are known as increasingly important (14). There are two underlying assumptions for the social benefits of mixed housing strategies: housing mix is strongly related to social mix, and social mix could create more social opportunities (2). And they serve as the theoretical underpinning of promoting housing mix in response to social issues deriving from poverty and segregation (14). In the literature, housing mix, concerning the attributes of housing units, is consistently referred as a mixture of different housing types or tenures (2). In comparison, social mix, emphasizing more on the characteristics of people, refers to a mixture of households of different socioeconomic positions, and often measured by the mixed level of income or occupational status (2, 15). Empirically, although studies have shown that housing homogeneity that create social homogeneity could reduce social opportunities for local residents, it is still debatable whether mixed housing strategies could create a social mix community and then nurture a positive socialization process that contributes to individual health outcomes.

Most discussions about housing mix or social mix and their social effects take place within the context of public housing, where socioeconomic disadvantage is implicated as a characteristic (3, 16). Public housing estates have been criticized for their contribution to poverty concentration and its concomitants, such as limited social opportunities, lack of necessary resources and social capital, negative socialization process, stigmatization effects, social disorder and even crimes (2, 8). Thus, social mix become a key target during public housing regeneration in many Western countries (17). Literarily, studies on the housing mix, social mix and their resultant social environment generate debatable and even conflicting points of view (15, 18). Supporters highlight social benefits that mixed communities can provide, including increased social interaction and opportunities, enhanced social networks and sense of community, reduced anti-social behavior, improved reputation, and liveability of the area, etc. (17, 19), while opponents note that mixing different groups together actually reveals a loosening of social bonds, reduces community, and social cohesion, but increases conflict (20). In light of these contrasting findings, establishing whether housing mix and social mix could

contribute to a higher quality of social environment within urban China requires careful examination.

2.2. Neighborhood social environment and mental health

The neighborhood effects of social environment on mental health has been discussed for decades in epidemiology, public health, and sociology discourses (21, 22). Extant studies on social environment and mental health suggest that social capital, strong social cohesion, high collective efficacy, and community participation could reduce the likelihood of depressive symptoms. However, lower levels of social cohesion, less cognitive social capital, and higher levels of neighborhood disorder, can all contribute to incidence of depression (23, 24). Within Chinese contexts, socialization process at local residence has been ascertained to be influential to population health, especially among particular groups. For example, social capital is found to be associated with suicidal ideation among Chinese college students (25); and local ties and trans-local ties are determinative to migrants' mental health, where social comparison and perceived social status serve as vital psychologically mediators (26). Accordingly, we focus on several frequently discussed constructs considered integral to neighborhood social environments and influential to residents' mental health, namely, social capital, social control, and a sense of community.

Arising from and implicated in everyday experiences and perceptions, social capital refers to "levels of social attachment among individuals indicative of social engagement and participation within communities" [(27), p. 104]. Many commentators consider social capital is able to affect personal health and to lead to health inequalities among different social groups (28). Scholars have various perceptions regarding the definition and measurement of social capital, and we adopt bonding social capital (social links between similar population) and bridging social capital (social links between dissimilar population) as two major dimensions, which are measured by cognitive factors (i.e., trust, social harmony) and structural factors (i.e., membership of networks), respectively (24, 29). Considering the ways in which social capital affects health, two prominent mechanisms are distinguished in literature: the compositional effect and the contextual effect (22). The former mechanism refers to that socially isolated people are more potentially to reside in neighborhoods lacking social capital, and such individuals are more easily to sustain poor health (30). For the latter, three plausible pathways are proposed: (1) by affecting people's health-related behaviors such as healthy-behavior norms, health-related information accessibility, and the exertion of social control over deviant behaviors (6); (2) by affecting people's accessibility to amenities and services which is related to the fact that cohesive neighborhoods are more likely to foster positive organizational processes that ensure good accessibility of the services and therefore are protective of health (22); and (3) by impacting psychosocial processes, as social capital could provide psychosocial resources such as self-esteem, affective support, and mutual respect that are protective of individual health (31).

As the widespread use of conventional behavioral indices to measure social capital cannot uncover the social and psychosocial processes that influence individual mental health (32), we further focus on the related psychosocial process of public housing by investigate residents' sense of community and social control. Public housing is often criticized for its inferiority in exerting sense of community and informal social control, which leads to high levels of social disorder and undermines residents' health and wellbeing (16). Sense of community can be a measure of the psychological basis upon which residents develop a willingness to intervene in community affairs (32), and it acts as the social process giving rise to informal social control (33, 34). Empirical evidence has suggested that psychological profits could accrue from experiencing a higher level of sense of community, and perceptions of health problems are linked with a lack of sense of community (35). Living in neighborhoods that lack order and social control may lead people to feel unsafe, mistrustful, powerless, isolated, angry, and anxious, all of which discourage outdoor activity and can result in mental health issues (3). By contrast, people who feel having control over their lives are more likely to increase their health conditions through health-enhancing behaviors, such as interacting with their surrounding environment in a positive way (3). Therefore, sense of community and social control are effective factors in explaining the mechanisms of social environment's influence on mental health, particularly the replenishment of the psychosocial pathways linking social capital and mental health.

2.3. Research hypotheses

Social environment characteristics intermediate the relationship between the levels of housing tenure mix and social mix and mental health is presented in Figure 1. Housing mix and social mix are regarded as structural determinants of health, which together shape neighborhood socioeconomic composition and cultural context. Social environment as a whole acts as an intermediate determinant between neighborhood structural factors and individual mental health. Sense of community and social control pertain to intermediate factors between the mixture status and residents' health, and social capital creates the association between housing/social mix and sense of community or social control. The following theoretical hypotheses are proposed:

H1: Housing tenure mix determines social mix and shapes the social environment characteristics.

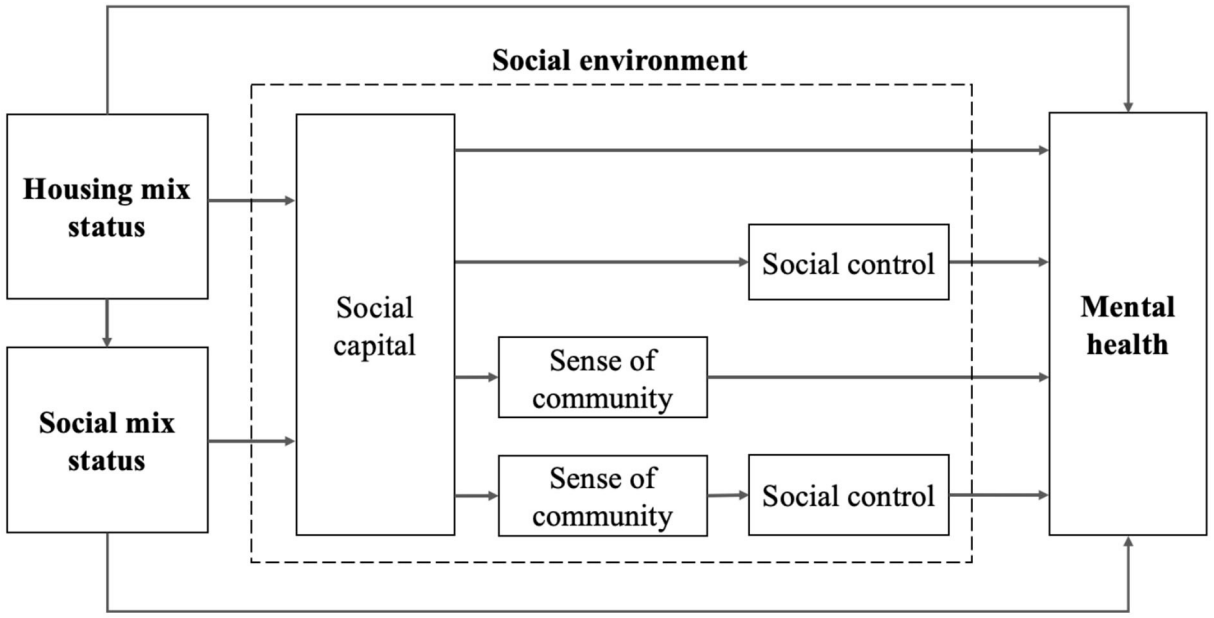

FIGURE 1
The conceptual framework.

H2: Housing tenure mix and social mix affect residents' mental health directly and indirectly.

H3: Social environment characteristics intermediate the relationship between the levels of housing tenure mix and social mix and mental health: (1) Social capital, sense of community, and social control are the mediators; (2) The mutual interactions between social capital, sense of community, and social control suggest a compound mediation mechanism.

3. Materials and methods

3.1. Case selection

Guangzhou was selected for the case study due to the innovative housing tenure mix the city has put in place over the last few decades. Since 2009 Guangzhou has adopted "measures for land reserve of public housing" and has regulated the lease of land by "controlling land prices but bidding on public housing." This housing tenure mix tool has been criticized for its economic benefit driven nature, since the provision of public rental housing has become a bargaining chip between developers and the local government during the land leasing process. Considering these evolved housing tenure mix tools, we choose six typical public housing projects developed at different times in urban Guangzhou to explore the associations of housing tenure mix with residents' mental health. Selection criteria included: development period and the specific political background, location, population scale, and most importantly, the level of housing tenure mix. Finally, three tenure groups of six neighborhoods are chosen as follows (Figure 2 and Table 1):

1) Private housing dominated neighborhoods: T and J housing estates. Both of them underwent a long development periods from the 1990s to the 2010s, throughout which period dominated housing tenure type has largely transferred from subsidized owner-occupied housing (i.e., economically affordable housing) to private-owned commodity housing *via* the transaction process in second-hand house market. T community was the earliest and the largest economically affordable housing estate in Guangzhou before 2002. By now, the ratios of commodity housing units in T and J are as high as 89.86 and 80.02%, respectively.
2) Public housing dominated neighborhoods: F, L, and Z housing estates. These neighborhood are mainly comprised of public rental housing (i.e., low-rent housing) and subsidized owner-occupied housing (i.e., economically affordable housing and joint-ownership housing). Commodity housing units are excluded in F and L and only take a small percentage (11.68%) in Z. Regarding the social objectives of these projects, Z has been regarded as a pioneering public housing project since 2008, because of its efforts on tackling housing shortages and improving quality-of-life for low-income

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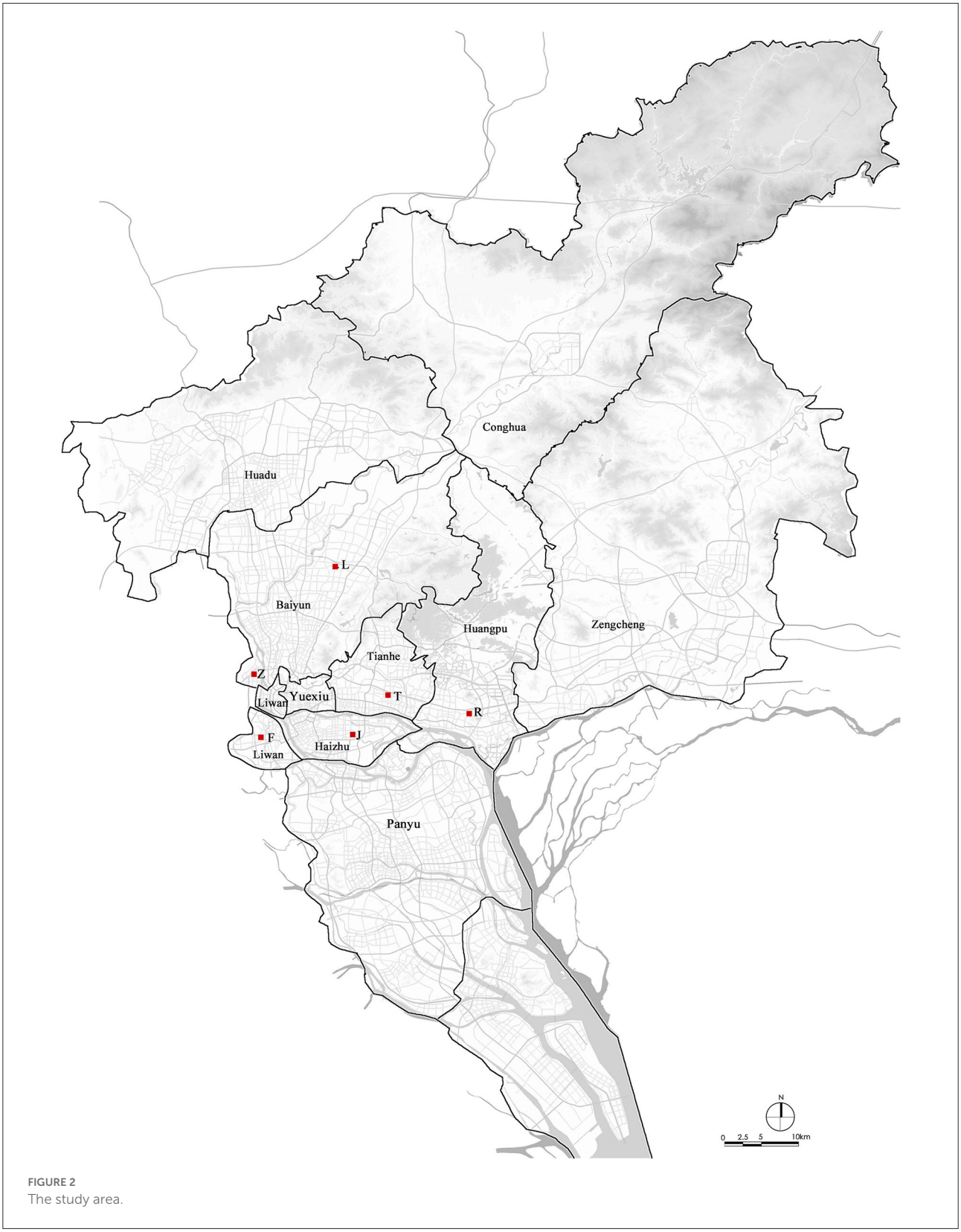

FIGURE 2
The study area.

populations. F has been developed as a benchmarking sample with relative high-end decoration and application of low-carbon technologies. L is the largest public housing estates in Guangzhou by now, playing an important housing security function.

3) Tenure-mixed neighborhood: R housing estate, developed with and promoted by urban renewal process, is representative in housing both original local residents and medium and low-income populations. So this neighborhood is comprised of balanced proportions of public rental housing (32.21%), subsidized owner-occupied housing (25.52%), and private-owned relocated housing units (42.27%).

3.2. Data collection

We administered a face-to-face questionnaire survey between 2nd and 16th June 2019. Three groups of datasets were collected: demographic and socioeconomic characteristics, perceived social environment characteristics, and mental health status. Respondents above the age of 18 who had been living in the housing estate for at least 1 year were selected, and consent was deemed to be granted by willingness to participate. Due to the difficulties in administering household surveys in gated communities, we collected data at the entrance of each housing estate by sampling one of every five passing residents. To improve sample representativeness, we referred to the ratios of each housing tenure type in each neighborhood during the sampling process, and conducted the survey during two time periods on weekdays and weekends. Survey data were collected using tablet computers. Finally, a total of 526 adults participated and 25 participants were removed from the sample due to invalid responses, such as providing exactly the same response to all items or providing incomplete responses to more than 20% of the items, leaving 501 valid surveys.

3.3. Variables

3.3.1. Housing tenure mix and social mix

The calculation of the entropy measure—a prominent measure for the nominal variables' variation—was adopted to measure mix levels. For housing tenure mix, three housing tenure types were classified according to housing tenure and homeownership: public rental housing, subsidized owner-occupied housing, and private housing. To measure social mix status, first, four household-income groups were identified: low-income family (<5,000 yuan), lower middle-income family (5,000–10,000 yuan), upper middle-income family (10,000–15,000 yuan), and better-off family (>15,000 yuan); second, three occupation positions were classified (job with high stability, job with low stability, unemployed). The proportions of each type of housing tenure and social status (income and occupation) relative to the total were computed, based on which the entropy measure was calculated according to Equation (1) and was standardized according to Equation (2):

$$H(x) = -\sum_i p_i \ln p_i \quad (1)$$

$$H'(x) = H(x) / \ln I \quad (2)$$

where pi is the likelihood of an observation pertaining to category i of X (neighborhood) and pi ln pi = 0 for pi = 0, and I is the maximum number of categories that the neighborhood has—since the figure of housing/income/occupation types vary per neighborhood (2).

This entropy measure runs from 0 to 1, with 0 implying absolutely no variation and 1 standing for absolute variation. Thus, five categories were identified: (1) absolutely homogenous (0); (2) homogeneous (0.01–0.25); (3) average homogeneity (0.25–0.50); (4) average heterogeneity (0.50–0.75); (5) heterogeneous (0.75–1.00).

3.3.2. Social environment: social capital, sense of community, social control

First, social capital was measured according to its two compositions: cognitive and structural social capital. Based on the social capital measurements developed by Lochner et al. (36), we developed a cohesion scale to measure the cognitive dimension of social capital and two questions on local friendship network and social participation to capture the attribute of structural social capital.

1) Cohesiveness: the cohesion scale comprised seven items on a 5-point scale. Respondents were asked to indicate how strongly they agreed or disagreed with the statements describing neighborly relations: (a) I know many neighbors in this community; (b) I frequently chat with my neighbors; (c) I visit my neighbors from time to time; (d) Neighbors can get help from each other; (e) This is a close-knit community; (f) Neighbors get along well with each other; (g) People are trustworthy in this community. The internal consistency was satisfactory (Cronbach's alpha = 0.864).
2) Local friendship network: measured by the proportion of friends within the neighborhood to total number of friends, with a higher score indicating a stronger connection to the neighborhood social network.
3) Social participation: this was measured by the average frequency with which respondents participated in three types of activities: (a) recreational activities; (b) activities organized by a residential committee or housing manager; (c) community committees. The mean score of these frequencies (rated by a 4-point scale) was calculated and higher score suggested higher frequency of social participation.

TABLE 1 Distribution of housing tenure types of the selected estates.

Tenure groups	T	J	F	L	Z	R
Public rental housing	10.09 (%)	13.96 (%)	32.81 (%)	61.62 (%)	60.07 (%)	32.21 (%)
Owner-occupied subsidized housing	0.04 (%)	6.02 (%)	69.19 (%)	38.38 (%)	28.25 (%)	25.52 (%)
Private housing*	89.86 (%)	80.02 (%)	0 (%)	0 (%)	11.68 (%)	42.27 (%)
Total units	8,888	6,528	5,935	12,298	5,918	5,992

Source: Guangzhou housing security office.
*Including both commodity housing and relocation housing.

Second, a sense of community scale consisting of 14-items was constructed, and respondents were asked to answer their perceptions on a 5-point scale with statements such as "When I leave this community for a while, I miss it very much" and "I'd love to invest my resources in this community, such as money and personal efforts." Given the internal consistency value of the items (Cronbach's alpha = 0.90), a single index of mean score was calculated, and higher score implied a greater perceived sense of community (35).

Third, social disorder, indicating that social control has broken down, was used as an indicative factor for measuring the level of collective efficacy of social control (37). Both social and physical signs can reflect the level of social disorder. To measure the level of informal social control, we asked respondents to report how often they had observed the following phenomena on a 5-point Likert-type scale: (1) physical signs (e.g., vandalism, litter, and graffiti); and (2) social signs (e.g., behavior that is harmful to society such as damaging public property and harassing neighbors; people or teenagers hanging around). Average scores were computed, with higher ones suggesting higher degree of collective efficacy of informal social control.

3.3.3. Mental health

We used the variable of mental wellbeing to evaluate individuals' mental health condition. Adult Mental Health Continuum Short Form (MHC-SF, Chinese version), which shows very good internal consistency ($\alpha > 0.80$) and discriminant validity in adults in various contexts, was adopted to establish residents' mental wellbeing. This scale is comprised of 14 items: three items for emotional wellbeing, six for psychological wellbeing, and five items for social wellbeing [(38); see the Supplementary Table 1]. Respondents were asked to evaluate how often they had experienced a particular feeling over the past 4 weeks according to six choices: "never," "once or twice," "once a week," "two or three times a week," "almost every day," and "everyday." The internal consistency of our data was satisfied (Cronbach's alpha of 0.899) and the mean score was computed to represent residents' mental wellbeing.

3.3.4. Covariate variables

Socioeconomic and demographic characteristics of the respondents were collected and regarded as the control variables in this study, including age, gender, marital, education, monthly household income, and occupation status.

3.4. Analysis strategy

Descriptive statistics were performed to capture the overall characteristics of the samples. Then to address the first research hypothesis, quick correlation analyses were conducted between housing mix status and social mix status, and between housing mix status and social environment variables. On the one hand, we used the Mantel-Haenszel Chi-square statistic to test the associations between housing mix status and income mix status, and housing mix status and occupation mix status. On the other hand, Spearman's correlation coefficients were computed for preliminarily identification of the correlative relations between housing mix status and social environment variables.

To address the second research hypothesis, we built a structural equation model according to the conceptual framework presented in Figure 1, examining the intermediatory roles of social environment variables between housing/income mix status and mental wellbeing. Besides the direct links among housing/income mix status, social environmental variables and mental wellbeing, the mutual interactions between the components of social environment variables were also accounted for, including the interaction between cognitive social capital and structural social capital, the influence of social capital on sense of community and social control, and the influence of sense of community on social control.

Furthermore, to explore the multiple mediation of social environment variables, we used the bias-corrected deviation correction method to evaluate the total, direct, and

indirect effects of two mix indicators and social environment variables on mental health. Then, the total indirect effects of housing mix status and social environment variables on mental health were broken down into specific indirect effects to identify the significant indirect paths. The analysis of mediation effect was carried out in the particular situation of repeated sampling 5,000 times by Bootstrapping, with a 95% confidence interval.

SPSS Statistics (version 24.0) and SPSS AMOS (version 24.0) software were employed to conduct correlation analysis and to construct path analysis models, respectively.

4. Results

4.1. Description of sample characteristics

The mean score for mental wellbeing was 4.50 (SD = 0.66) on a 6-point scale. Referring to the diagnostic criteria that respondents must experience "every day" (scored as 5) or "almost every day" (scored as 6) to indicate the status of flourishing mental health, the average mental health condition of the participants did not reach the flourishing level (38).

Summarizing the socioeconomic and demographic characteristics of samples, the sex ratio was 1:1, and age ranged from 18 to 86 years old, averaging 37 (SD = 12.90). The ratios of married and college-educated were 64.87 and 48.32%, respectively. Around half (49.70%) reported a monthly household income of 5,000–10,000 RMB/month, and 64.87% had formal and stable jobs.

Summarizing the characteristics of residential property, 68.46% of respondents were public rental housing tenants, 17.37% were subsidized homeowners, and the average duration of residency was 4.93 years. Different mixture levels of housing tenure were unfolded: LG (H = 0) and TD (H = 0.37) were homogeneous, while JSZ (H = 0.54), JD (H = 0.73), RD (H = 0.75), and FH (H = 0.99) were heterogeneous. To the contrast, the entropy measures of income and occupation mix suggested that all neighborhoods were socially heterogeneous.

Regarding the attributes of social capital, the average score of cohesiveness was 3.45 (SD = 0.70), suggesting a relatively cohesive social environment for cultivating social capital at the neighborhood level. The mean of closure of social network was 0.36 (SD = 0.20), and the average score for social participation was 1.93 (SD = 0.74), indicating that respondents seldom participated in collective activities. Sense of community and social control were both between a neutral and positive status (M = 3.40, SD = 0.52; M = 3.49, SD = 0.71), suggesting a slightly positive person–place emotional attachment and functional dependence, and a relatively low occurrence frequency of social disorder.

4.2. Preliminary correlations analyses: Housing mix, social mix, and social environment

We used Mantel-Haenszel Chi-square tests to check for the linear relation between housing tenure mix status and social mix status (the former was assigned an entropy value of housing tenure and homeownership type; the latter was assigned two entropy values of income and occupation). Results of the linear-by-linear association test of trend suggested a strong linear relationship between housing tenure mix and income mix ($\chi^2 = 403.133$, $p < 0.001$; Pearson's $R = 0.898$, $p < 0.001$), indicating that a higher level of housing tenure mix could contribute to a higher level of income mix. By contrast, the Mantel-Haenszel Chi-square statistic showed no significant linear relationship between housing tenure mix and occupation mix ($\chi^2 = 0.905$, $p = 0.341$), suggesting that housing tenure mix status had no effect on the mix level of occupation stability in this data. So we used income mix status to indicate social mix in the following statistical analyses.

Regarding the correlation between housing tenure mix and social environment, results of Spearman's correlation analysis indicated that: (1) housing tenure mix status was significantly, but weakly, associated with cohesiveness (rs = 0.182, $p < 0.001$) and social participation (rs = 0.369, $p < 0.001$); (2) but no significant correlation was found between housing tenure mix status and local friendship network (rs = −0.087, $p = 0.053$), sense of community (rs = 0.053, $p = 0.233$), and social control (rs = 0.085, $p = 0.057$). Similarly, results of Spearman's correlation analysis between income mix status and social environment variables suggested that: (1) income mix status was also significantly, but weakly, associated with cohesiveness (rs = 0.206, $p < 0.001$) and social participation (rs = 0.266, $p < 0.001$); (2) but no correlation was found between income mix status and local friendship network (rs = −0.084, $p = 0.059$) or social control (rs = 0.060, $p = 0.182$); (3) while income mix status was significantly, and very weakly, associated with sense of community (rs = 0.117, $p = 0.009$). Consistently, the correlation relationship of each variable has been visualized with the help of heatmap (Supplementary Figure 1). Accordingly, the links between housing tenure mix status and its uncorrelated social environment variables, and the links between income mix status and its uncorrelated social environment variables were not accounted for in the path analysis model.

4.3. Pathways between housing mix, social environment, and mental health

Goodness of fit of the path analysis model was assessed through Chi-Square/df (<3 good, <5 permissible; $p > 0.05$, CFI >= 0.90, GFI > 0.95, AGFI >0.90, RMSEA < 0.08), according

to which our path analysis model showed satisfactory fitness for this data ($\chi^2/df = 1.685$, $p = 0.034$, CFI = 0.992, GFI = 0.990, AGFI = 0.957, RMSEA = 0.037). Standardized coefficients with their statistical significance are reported in Figure 3 and Table 2, showing all pairwise paths among variables in the model. The total direct and indirect effects of independent variables on mental wellbing are summarized in Table 3.

Results suggested that housing tenure mix status impeded respondents' mental wellbeing significantly and directly (Std estimate = −0.214, $p = 0.024$), but it contributed to mental wellbeing in terms of total indirect influences (Std estimate = 0.231, $p = 0.005$). However, the total effect of housing tenure mix on mental wellbeing was not significant in this data. By contrast, income mix status had neither direct nor indirect influence on mental wellbeing (Std estimate = 0.132, $p = 0.160$; Tables 2, 3). Further, a significantly profound effect of housing tenure mix status on income mix status was confirmed (Std estimate = 0.898, $p < 0.001$), consistent with the above inference about the strong predictive power of housing tenure mix status for social mix status.

Regarding the total, direct, and indirect effects of social environment variables on mental wellbeing: (1) on the whole, cohesiveness played the most important protective role of enhancing mental wellbeing (Std estimate = 0.265, p<0.001), followed by social participation (Std estimate = 0.159, $p = 0.003$), sense of community (Std estimate = 0.126, $p = 0.009$), and social control (Std estimate = 0.113, $p = 0.012$); whereas local friendship network had an adverse effect on mental wellbeing (Std estimate = −0.166, $p = 0.001$); (2) cohesiveness, social participation, and sense of community produced positive direct and indirect effects on mental wellbeing; local friendship network impeded mental wellbeing directly (Std estimate = −0.184, $p < 0.001$), but slightly contributed to mental wellbeing by indirect pathways (Std estimate = 0.080, $p = 0.049$), and social control contributed to mental wellbeing directly (Table 3).

Furthermore, we essentially broke down the total indirect effects of housing tenure mix on mental wellbeing into the specific indirect effects that were significant and non-significant. According to the standardized estimate of the path coefficients, the most important indirect path linking housing mix status to mental wellbeing flows through social participation (Std estimate = 0.121, $p = 0.004$). The full path linking housing tenure mix status, social participation, sense of community, social control, and mental wellbeing was also significant, but the coefficient was quite small (Std estimate = 0.001, $p = 0.049$), indicating very weak indirect impact (Supplementary Table 2).

Regarding specific indirect effects of social environment variables on mental wellbeing, 18 paths were examined. Although effects were slight, we found that: (1) structural social capital, sense of community, and social control played significant mediating roles between cohesiveness and mental wellbeing; (2) sense of community played protective mediating roles between social capital and mental wellbeing; (3) social control played protective mediating roles between cohesiveness and mental wellbeing, and between sense of community and mental wellbeing (Supplementary Table 3). We thus confirm the compound paths between social environmental variables and mental wellbeing, which are induced by the mutual interactions among social capital, sense of community, and social control.

5. Discussion

5.1. Social effects of housing tenure mix

Regarding Hypothesis 1, we proved that housing tenure mix had profound impacts on social mix partially, and moderate effects on social capital partially as well. Given the strong positive association between housing tenure mix and income mix, we believe that housing tenure mix can promote social mix partially. This intrinsically causal association could be driven by the original intention of Chinese housing mix policy, which primarily focused on adjusting housing prices through combining public housing and commodity housing units (10, 39). Diversified tenure types are encouraged by the government's involvement in the owner-occupied section, such as subsidized housing owners, housing owners in *Danwei* communities, and tenants of public rental housing, making it reasonable to construct a mixture of families with different income statuses (40). However, diverging from some findings in the Western context in terms of the positive effects of housing tenure mix on occupation mix (15), we found no association between them. This may indicate that housing tenure mix policy has played little role in increasing social opportunities or promoting social mobility, since individuals' employment position is often considered to adequately indicate their social opportunities (2).

This study also adds additional evidence on the positive effects of housing tenure mix on structural social capital, by noting that housing tenure mix may lead to more opportunities for social interactions and participations. Disadvantaged and declining neighborhoods usually hinder residents' willingness to take part in collective activities, on the countrary, better-off community socioeconomic status is a strong determinant of social participation (41). Housing tenure mix has significantly improved the socioeconomic status of the communities in our study, since nearly 50% of our respondents were college-educated and nearly half reported a household income of 5,000–10,000 RMB per month. And the improved socioeconomic position could contribute to increased structural social capital (20). Responding to the previous accusation that housing tenure mix serves as an economic driver rather than a social stabilizer in public housing development (13), we may refute this argument partially by demonstrating the positive influence of housing tenure mix on social participation, which is an important component comprising social capital. But it should also be noted that the improved community socioeconomic position could

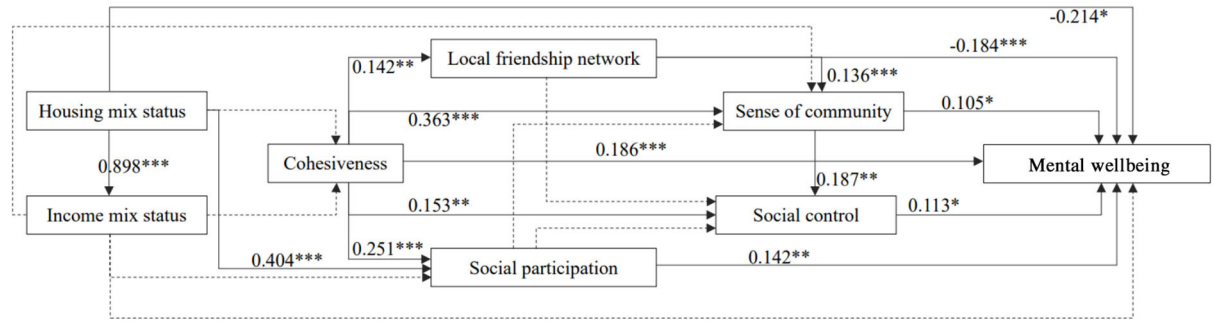

FIGURE 3
The standard coefficients of the pathway.

TABLE 2 Direct paths among variables of housing and social mix, social environment, and mental wellbeing (standardized estimates, N = 501).

Path	Std estimate	S.E.	*p*
Income mix status <–Housing tenure mix status	0.898***	0.005	0.000
Cohesiveness <–Income tenure mix status	0.115	0.891	0.239
Cohesiveness <–Housing tenure mix status	0.129	0.220	0.185
Social participation <–Income tenure mix status	− 0.116	0.878	0.204
Social participation <–Housing tenure mix status	0.404***	0.217	0.000
Sense of community <–Income tenure mix status	0.029	4.372	0.499
Social participation <– Cohesiveness	0.251***	0.044	0.000
Local friendship network <– Cohesiveness	0.142**	0.013	0.001
Sense of community <– Cohesiveness	0.363***	0.484	0.000
Sense of community <– Social participation	0.077	0.451	0.082
Sense of community <– Local friendship network	0.136***	1.586	0.000
Social control <– Cohesiveness	0.153**	0.049	0.002
Social control <– Local friendship network	0.012	0.153	0.791
Social control <– Social participation	0.068	0.043	0.134
Social control <– Sense of community	0.187***	0.004	0.000
Mental wellbeing <– Housing tenure mix status	−0.214*	0.202	0.024
Mental wellbeing <– Income mix status	0.132	0.802	0.160
Mental wellbeing <– Cohesiveness	0.186***	0.045	0.000
Mental wellbeing <– Local friendship network	−0.184***	0.138	0.000
Mental wellbeing <– Social participation	0.142**	0.041	0.002
Mental wellbeing <– Sense of community	0.105*	0.004	0.023
Mental wellbeing <– Social control	0.113*	0.041	0.010
Mental wellbeing <– Age	−0.132*	0.003	0.011
Mental wellbeing <– Sex	−0.009	0.055	0.829
Mental wellbeing <– Education	0.078	0.032	0.100
Mental wellbeing <– Marital status	0.016	0.060	0.734

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

TABLE 3 Total, direct, and indirect effects of independent variables on mental health wellbeing (Std estimate, N = 501).

		Housing mix status	Income mix status	Cohesiveness	Local friendship network	Social participation	Sense of community	Social control
Mental health	Direct effect	−0.214*	0.132	0.186***	−0.184***	0.142**	0.105*	0.113*
	Indirect effect	0.231**	0.016	0.080**	0.018*	0.017*	0.021**	-
	Total effect	0.017	0.148	0.265***	−0.166**	0.159**	0.126**	0.113*

*p < 0.05, **p < 0.01, ***p < 0.001.

probably be caused by the inflow of target groups such as the newly emerging middle class, rather than as a natural result of local development (11). Therefore, the selection effect of housing tenure mix on forming community socioeconomic structures should be considered when determining the effectiveness of housing mixed strategy and requires further research.

5.2. Mental health effects of housing tenure mix

In relation to Hypothesis 2 and 3, that on the whole, neither housing tenure mix nor income mix affected mental health significantly; rather, housing tenure mix thwarted mental health in a direct way but contributed to it in an indirect way through promoting social participation. Housing tenure mix impaired mental health directly, which differs from some Western evidence supporting the hypothesis that mixed tenure can benefit individual of various dimensions (20). Considering the trend of housing capitalization in urban China, we suspect that housing tenure mix makes it difficult for mixed community residents to develop positive psychological cognition due to the poverty metaphor attached to public housing. Unlike the West's practice whereby public housing units are increasingly being designed to be externally indistinguishable from market-rate units (42), the public housing units in our study were explicitly identified as such by signs on the building facades, so such tenants could easily be differentiated from commodity housing residents. Further, those living in public housing are often stigmatized by the media and in the minds of the public in general for their reliance on government subsidies and perceived self-destructive and non-mainstream behaviors (33, 42). On this basis, various social conflicts exist between public housing tenants and commodity housing homeowners regarding public facilities and open space, property fees, and related management services, which has been reported often in local news. Thus, the poverty and backwardness metaphor of public housing and its related social stigma undermine the development of positive psychological cognition toward mixed-housing communities. Further, this study confirms the mediating role of social capital between housing tenure mix and mental health, of which underlying social mechanisms are demonstrated as follows.

5.3. Social mechanisms for mental health

Considering the intermediatory role of social environment variables, this study identifies the direct health impact of social capital, as well as mediation of sense of community and social control between social capital and mental health. Accordingly, the behavioral, psychological, and mutually interactional mechanisms of social environment variables influencing mental health were revealed.

Social participation, as a health-related behavior, improves mental health on a behavioral mechanism basis. Consistent with established arguments, social participation is helpful for forming social networks that communicate information and share resources, providing social support, and establishing social norms, which are conducive on health grounds (9, 31). Increasing social participation means more opportunities to interact with diverse neighbors, and one can obtain more information, have more opportunities to gather resources and affective support, and gain mutual respect and self-esteem during these social activities. In comparison, cohesiveness and sense of community were protective for mental health on a psychological mechanism basis, such as through reducing a person's risk of social exclusion (43), increasing emotional sustenance to alleviate the emotional impacts of stressors (44), and providing individuals with meaningful social connections and enhancing self-esteem (22).

Behavioral and psychological mechanisms are usually intertwined with each other, affecting residents' health synergistically. Specifically, cohesiveness could protect individual health by promoting emotion sustaining behaviors and instrumental aid from neighbors (44). Further, a lack of social control could result in cognition of a threatening environment and resultant feelings of unsafe, powerless, isolated, anxious, and depressed, as well as discourage health-enhancing behaviors, which all impede residents' mental health (3). During the field trips, a significant amount of litter, abandoned furniture, vandalism, and run-down buildings

were observed in JD and TD, which may suggest that the residents may not respect the properties they live in and these communities showed incapability of dealing with local problems (45). Thus, lacking social control can threat residents' mental health in two ways: first, signs of disorder could induce the psychophysiological response it engenders. Repeated exposure to disorder and a threatening environment put people under frequent and intense stress response status, which can, in turn, erode mental health. Second, people whose lives are under control have a high possibility to take health control and health-enhancing behaviors, such as enhancing physical activities and interacting with their surrounding environment in a positive way (3, 45).

Based on the transactions between social environment variables, socially interactional mechanisms are proposed, highlighting the mediation of sense of community and social control between social capital and mental health. Social capital is found to be greatly conducive to the growth of sense of community, which echoes the established viewpoint that sense of community, as integral to sustaining a community, is a correlate of social capital (46). Sense of community has been ascertained to be affected by several aspects of social environment, including neighborhood cohesion and satisfaction, community ties and support, and participation in community organizations (34). Our findings support this viewpoint by revealing that cohesiveness and connections with local social networks can contribute to sense of community.

Social control intermediates the relationship between cognitive social capital and mental health. Cohesiveness could assist residents maintain informal social control by providing mutual support among neighbors and reducing the number and extent of the stressors that residents perceive in neighborhoods (47). Cohesiveness is also a precursor to community problem-solving because it can increase the likelihood that residents care about the community and are able to achieve consensus in relation to both acknowledging and addressing community problems (48). However, structural social capital had little impact on social control in this study. Although previous studies propose that local friendship networks could promote social control by helping residents to recognize strangers and enabling guardianship behaviors (49), and social participations can mitigate victimization and delinquency (50), this study finds that having local friends and participating in collective activities may not be enough to enable the communities to exercise social control. A possible explanation may be that: their seeming irrelevance to social control may be derived from the spirit of the golden mean as expressed by the Chinese philosophy of Confucianism (namely Middle, "中庸" in Chinese). Following the standard of moderation, people would act prudently when interfering in the behavior of others, which explains the non-existent impact of structural social capital on social control in this study.

Also, social control serves as a mediator between sense of community and mental health. Sense of community can benefit the degree to which residents work together on common public problems, fostering the community's ability to exercise informal social control (51). For the declining appearance of the residential environment, sense of community may nurture the community's ability of improving the living environment and benefiting residents' mental health accordingly.

Lastly, we found contradictory effects of connections with local friendship networks on mental health between direct and indirect pathways. Although connections with local friends indirectly contributed to mental health through increasing sense of community, there was much stronger negative associations between local friendship networks and mental health. Concerning the measurement of local social networks we used, which indicates the diverse social, cultural, and ecological contexts where residents are embedded, higher level of local friendship network refers to lower level of friendship heterogeneity (52). People who depend on a local friendship network may have less support than those with diverse and heterogenous social networks, which is not conducive to protecting personal health (53). It is thus reasonable that the social network developed within the mixed communities may be inadequate and not strong enough to fully support the residents.

6. Conclusion

With empirical evidences from Guangzhou, we ascertained that housing tenure mix influenced residents' mental health in either direct or indirect ways with opposite effects: it threatened residents' mental health directly; meanwhile, it improved neighborhood social capital *via* increasing the opportunities of social participation, which further contributed to residents' mental health. For the underlying social mechanisms affecting mental health, we unfolded that: on the one hand, the positive psychosocial process engendered by cohesiveness and sense of community can protect individuals from psychological issues. Cohesiveness and sense of community determine better social control, thereby giving rise to improved mental health, albeit indirectly. On the other hand, social participation and social control play proactive roles in mental health on a behavioral mechanism basis. Considering social capital as a complete indicator, the contradictory health effects of structural social capital are displayed, suggesting the potentially complicated influence of social capital on health.

To summarize, future housing mix strategies should look on their implications for the positive social environment that would be proactive in fostering residents' mental health. We propose that there will be significant mental health benefits if housing mix intervention paid more attention on the improvement of the quality of social environment, specifically, promoting neighborhood cohesion, strengthening a sense of community, and forming high level of informal social control. Additionally,

we propose that there should be an "ideal" level of housing tenure mix for maximizing social and health benefits, a question which should be further explored and determined for the future mixed housing strategies.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

TZ and XL: conception and design of the study and drafting the manuscript. TZ: acquisition of data. TZ and JL: analysis and/or interpretation of data. TZ, XL, and JL: revising the manuscript critically for important intellectual content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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Associations of road traffic noise and its frequency spectrum with prevalent depression in Taichung, Taiwan

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Introduction: Exposure to road traffic noise has been reported to be associated with depression in many epidemiological studies, but the association between noise frequency spectrum and depression remains unclear. This community-based study investigated the associations between road traffic noise exposure and its frequency components with prevalent depression.

Methods: A total of 3,191 residents living in Taichung who participated in the Taiwan Biobank between 2010 and 2017, were included as study participants. The land-use regression models were used to evaluate individual annual average values of A-weighted equivalent sound level over 24 h ($L_{eq,24h}$) and particulate matter with an aerodynamic diameter <2.5 μm ($PM_{2.5}$) using the geographic information system. Multiple logistic regression was applied to estimate the odds ratios (ORs) for depression after adjusting for potential risk factors and $PM_{2.5}$.

Results: An interquartile range increase in $L_{eq,24h}$ at full frequency (4.7 dBA), 1,000 Hz (5.2 dB), and 2,000 Hz (4.8 dB) was significantly associated with an elevated risk for depression with ORs of 1.62 (95% confidence interval [CI]: 1.03, 2.55), 1.58 (95% CI: 1.05, 2.37), and 1.58 (95% CI:1.03, 2.43), respectively, by controlling for $PM_{2.5}$. The high-exposure group (≥3rd quartile median of noise levels) at full frequency, 1,000 Hz, and 2,000 Hz had an increased risk for depression with ORs of 2.65 (95% CI: 1.16–6.05), 2.47 (95% CI: 1.07–5.70), and 2.60 (95% CI: 1.10–6.12), respectively, compared with the reference group (<1st quartile of noise levels) after adjustment for $PM_{2.5}$. Significant exposure-response trends were observed between the prevalent depression and noise exposure by quartiles at full frequency, 1,000 Hz, and 2,000 Hz (all $p < 0.05$).

Conclusion: Exposure to road traffic noise may be associated with an increased prevalence of depression, particularly at 1,000 and 2,000 Hz.

KEYWORDS

cross-sectional study, depression, final particles, noise spectrum, prevalence, road traffic noise

1. Introduction

Mental disorders are a major global health concern. According to a World Health Organization (WHO) report in 2015, over one-third of the global population suffers from mental disorders annually, and the most common symptoms are depression and anxiety (1). The global burden of mental disorders continues to increase, causing considerable social and economic loss. Mental health is affected by environmental exposure and individual factors, such as genes, demographic characteristics, lifestyle, and socioeconomic status (2). The World Health Organization reports that the global population living with common mental disorders is estimated to be 4%, including 322 million people with depression (3).

Noise is defined as an uncomfortable or unwanted sound that can cause physical damage or psychological harm through various biological mechanisms (4). Exposure to noise activates the acoustic nerve to disturb the related structures in the central nervous system, such as the hypothalamic-pituitary-adrenal (HPA) axis, which is regarded as an endogenous pathway between noise and depression (5, 6). In addition, exposure to road traffic noise may affect the central nervous system and brain to increase the risk of neuropsychiatric disorders, including depressive symptoms, anxiety disorder, impaired cognitive function, dementia, and stroke (7). Noise also can cause annoyance or other negative emotions to induce psychophysiological stress responses that are related to depression (6, 8).

Many epidemiological studies have found an association between exposure to road traffic noise and depressive symptoms (9, 10). A longitudinal study reported that one A-weighted decibel (dBA) increase in daytime was significantly associated with the elevated risk on emergency hospital admissions of depression (11). A 5-year follow-up study observed that residents exposed to a 24-h noise level >55 dBA had a significantly higher risk of depressive symptoms compared with those exposed to ≤55 dBA (10). A case-control study revealed that inhabitants exposed to road traffic noise at a 24-h noise level ≥70 dBA had a significantly higher risk of depression (12). Subjects exposed to a road traffic noise level ≥70 dBA in day-evening-night level (Lden) showed a significantly increased prevalence of depression mood compared with those exposed to 45–54 dBA in a cross-sectional study (9). Although two meta-analysis studies concluded the low-quality evidence of road traffic noise exposure associated with medication use and interview measures of depression (13, 14), the latest review observed a marginal but not signficant elevated risk for depression per 10 dBA in Lden (15).

Different noise frequencies may be associated with the varying effects on health. Environmental noise frequencies of 63, 125, and 1,000 Hz were significantly associated with the prevalent hypertension among residents (16). Two cross-sectional studies reported the association between exposure to low-frequency noise at 10–250 Hz with annoyance (17, 18). The methods used to control the different noise levels rely on their frequency components (i.e., noise insulation for high frequencies and sound absorption for low frequencies). However, the association between frequency spectrum of road traffic noise and depression remains unclear.

In addition to road traffic noise exposure, traffic-related particulate pollutants may be associated with the depression. Previous studies have reported an association between exposure to particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) and an increased risk of depression (19–21). A cross-sectional study had found the association between one interquartile range (IQR) increase in $PM_{2.5}$ levels (0.83 $\mu g/m^3$) and an elevated prevalence of psychological distress after adjusted for road traffic noise (22), but the relationship between frequency components and depression were not investigated. To the best of our knowledge, no study has been performed to elucidate the association between noise frequency spectrum and depression. Therefore, two hypotheses were determined in the present study: (i) exposure to road traffic noise was associated with the increased risk of prevalent depression independently excluding the confounding effect of $PM_{2.5}$; (ii) such association between road traffic noise exposure and prevalent depression was higher at low-to-medium frequencies than that at other frequency components. This study aimed to investigate the associations between road traffic noise exposure and its frequency components and the prevalence of depression after adjustment for $PM_{2.5}$ in Taichung, Taiwan.

Abbreviations: CI, confidence interval; IQR, interquartile range; L_{eq}, equivalent sound levels; LUR, land-use regression; ORs, odds ratios.

2. Materials and methods

2.1. Study population

This community-based cross-sectional study relied on the Taiwan Biobank database, which is a national project to systematically collect information from 125,221 inhabitants aged 30–70 years in the Taiwanese population through 29 recruitment centers, including their environmental factors, lifestyles, biomarkers, and clinical medical examinations from 2006 to 2019 in Taiwan (23, 24). Because the noise exposure was available to predict retrospectively from 2010 in Taichung city, only 3,201 residents living in Taichung city were included from the Taiwan Biobank. Nine subjects who did not provide completed questionnaire information and one participant who entered the database in 2009 were excluded. Finally, the total number of study participants was 3,191 adults (1,597 men and 1,594 women) who lived in Taichung city and participated in the Taiwan Biobank from 2010 to 2019.

The study protocol was reviewed and approved by the Central Regional Research Ethics Committee of China Medical University, Taichung, Taiwan (protocol number: CRREC-108–006). Each subject provided the written informed consent.

2.2. Definition of depression cases

A self-administered questionnaire released by the Taiwan Biobank was used to obtain individual data on potential risk factors for depression. These factors included age, sex, height, weight, lifestyles (such as cigarette smoking, alcohol consumption, and regular exercise), and a family history of depression. Participants were regarded as having depression if an individual answered the question: "Have you been diagnosed with depression by a physician?" In addition, participants were defined as having a family history if they answered the question, "Has your mother/father been diagnosed with depression by a physician?" at the baseline survey.

2.3. Exposure assessments

Based on participants' residency, we estimated the annual levels of road traffic noise and $PM_{2.5}$ at the urban district level in Taichung city by the land-use regression method. The land-use regression (LUR) models of road traffic noise (25) and $PM_{2.5}$ (26) established in previous studies were used to estimate individual exposure levels retrospectively when participants joined the Taiwan Biobank at baseline. The LUR model-explained variance (R^2) of the road traffic noise for the full frequency was 83%, with the highest R^2 of 0.88 at 250 Hz and the lowest R^2 of 0.67 at 31.5 Hz. The precision for the full frequency was 2.09 dBA with the highest

precision (2.59 dB) at 31.5 Hz and the lowest precision (1.89 dB) at 250 Hz. The accuracy for full frequency was 4.4 dBA with the highest accuracy of 6.9 dB at 1,000 Hz and the lowest accuracy of 3.6 dB at 250 Hz (25). The LUR model explained variance (R^2) for $PM_{2.5}$ was 0.53 with a precision of 10.2 $\mu g/m^3$ and an accuracy of 103.9 $\mu g/m^3$ (26). Since individuals had entered the Taiwan Biobank at different periods, the annual means of road traffic noise and $PM_{2.5}$ exposures were adjusted for the difference between annual averages at six noise and five air-quality monitoring stations, which were setup by the Taiwan Environmental Protection Agency.

A geographic information system (ArcGIS 10.3, ESRI, Redlands, California, United States of America) was applied to integrate the parameters of land-use types, road area, road length, population numbers, and the major emission sources at different buffers to estimate the annual means of road traffic noise and $PM_{2.5}$ for each participant between 2010 and 2019.

Based on the environmental exposure assessments, the participant were divided into four exposure groups by quartile (i.e., <1st quartile, 1st-2nd quartile, 2nd-3rd quartile, and ≥3rd quartile) in order to have the same number of subjects in each group for different frequency comparisons and tests of exposure-response trends. The median exposure level of $PM_{2.5}$ was 33.0 $\mu g/m^3$. In addition, the per 1-IQR increase in continuous noise variables was applied to determine the association with depression among residents in Taichung.

2.4. Statistical analysis

The Kolmogorov-Smirnow test was conducted to exam the normality of continuous variables for studying the association between road traffic noise exposure and prevalent depression because of sample sizes were >50. Univariate comparisons were performed using The Wilcoxon rank-sum test and the chi-square test were applied to perform univariate comparison for continuous variables and categorical variables, respectively. Spearman's correlation coefficients were calculated to exam the correlation between the road traffic noise and $PM_{2.5}$. Logistic regression models were used to estimate ORs and 95% CIs for investigating the association between noise exposure and depression. Change-in-estimate was provided to select co-variables by trial and error for the multiple regression (27), and risk factors in multiple regression, which have an increased effect >3%, were selected to enter the models.

Single exposure variables of 24-h road traffic noise and its frequency components were built as Model 1 to estimate the risk of prevalent depression. All possible risk factors (such as age, sex, body mass index, diastolic and systolic blood pressure, alcohol consumption, betel nut chewing habits, cigarette smoking, current employment, regular exercise within the past 3 months, marital status, family history of depression, education level, monthly self-income, and monthly family income) were added to Model 1 to determine a 3% increase in the ORs of the exposure variable until no more variables exceeded this criterion. Regular exercise within 3 months, cigarette smoking, and monthly personal income were added to Model 2. Three variables to present biological plausibility, namely age, sex, and body mass index, as well as related risk factors of alcohol drinking (28), marital status (29), and a family history of depression (30) were combined with Model 2 to generate Model 3. Finally, $PM_{2.5}$ levels were added to Model 3, accounting for the interaction to create the final model (i.e., Model 4). All analyses were conducted using the SAS standard package for Windows version 9.4 (SAS Institute Inc., Cary, North Carolina, USA). The significance level was set at a $p < 0.05$ for all statistical tests.

3. Results

Table 1 shows the demographic characteristics of the study participants in the Taiwan Biobank from 2010 to 2019. Significant differences were identified between depressive and non-depressive groups in body mass index, sex, marital status, currently employed, monthly self-income, and family history of depression (all $P < 0.05$).

Table 2 presents the annual mean values of the 24-h road traffic noise and $PM_{2.5}$. The annual mean of $L_{eq,24h}$ for full frequency was 68.12 ± 3.74 dBA, with the highest value of 64.47 ± 4.24 dB at 1,000 Hz. The annual mean concentration of $PM_{2.5}$ was 32.39 ± 5.38 $\mu g/m^3$ and ranged from 17.68 to 46.98 $\mu g/m^3$.

The correlations between the annual 24-h road traffic noise and $PM_{2.5}$ are shown in Table 3. The $PM_{2.5}$ level was significantly correlated with 24-h road traffic noise levels at full (correlation coefficient = 0.339) and spectrum frequencies (all $P < 0.001$), which was observed with the highest correlation (coefficients = 0.636) at 31.5 Hz and with the lowest correlation (coefficients = 0.173) at 31.5 and 250 Hz, respectively.

The associations between an interquartile range (IQR) increase in annual 24-h road traffic noise and prevalent depression are shown in Table 4. An IQR increase in full frequency (4.7 dBA), spectrum frequency at 1,000 Hz (5.2 dB), and frequency component at 2,000 Hz (4.8 dB) were significantly associated with an increased risk of depression (OR = 1.62, 95% CI: 1.03–2.55; OR = 1.58, 95% CI: 1.05–2.37; OR = 1.58, 95% CI: 1.03–2.43) after adjusting for potential risk factors and $PM_{2.5}$.

Table 5 presents the associations between dichotomous noise exposure groups (by quartile) and prevalent depression. The OR for prevalent depression was significantly higher in high-exposure group (≥3rd quartile, Q3) at the full frequency and spectrum frequencies of 1,000 and 2,000 Hz compared with the reference group (<1st quartile, Q1) after controlling for potential risk factors and $PM_{2.5}$. Participants exposed to ≥71.4 dBA at full frequency, those exposed to ≥68.0 dB at 1,000 Hz, and those exposed to ≥65.7 dB at 2,000 Hz had significantly higher risks of 2.65 (95% CI: 1.16–6.05), 2.47 (95% CI: 1.07–5.70), and 2.60 (95% CI: 1.10–6.12) than the reference groups, respectively. Significant exposure-response trends were identified between the prevalent depression and the stratum of noise exposure at full frequency (OR = 1.40, 95% CI: 1.09–1.79, $p = 0.009$), 1,000 Hz (OR = 1.37, 95% CI: 1.06–1.77, $p = 0.015$), and 2,000 Hz (OR = 1.42, 95% CI: 1.09–1.84, $p = 0.009$).

We also conducted the analyses of interaction effects between road traffic noise (including different frequency components) and $PM_{2.5}$, but no significant interaction effects were observed (all $p > 0.05$) after adjusting for age, sex, BMI, cigarette smoking, alcohol drinking, married status, monthly self-income, regular exercise within 3 months, and family history.

TABLE 1 Demographic characteristics of study participants in Taiwan Biobank from 2010 to 2019.

Characteristics	Depression ($n = 102$)	Non-depression ($n = 3,089$)	*P*-value
Age (year), mean (SD)	48.51 (11.37)	47.96 (11.10)	0.600[a]
BMI (kg/m^2), mean (SD)	23.78 (3.97)	24.39 (3.79)	0.046[a]
Sex, male (%)	40 (39.22)	1,557 (50.40)	0.026[b]
Education level, >12 years (%)	54 (52.94)	1,291 (41.79)	0.289[b]
Marriage, yes (%)	17 (16.67)	415 (13.43)	<0.001[b]
Divorced or widow, yes (%)	23 (22.55)	288 (9.32)	<0.001[b]
Currently employed, yes (%)	23 (22.55)	849 (63.36)	0.003[b]
Monthly self-income, >30,000 NTD (%)	19 (18.63)	847 (27.48)	0.049[b]
Monthly family income, >80,000 NTD (%)	18 (17.65)	555 (17.97)	0.934[b]
Cigarette smoking, yes (%)	19 (18.63)	381 (12.33)	0.056[b]
Alcohol consumption, yes (%)	12 (11.76)	266 (8.61)	0.268[b]
Betel-nut chewing, yes (%)	3 (2.94)	88 (2.85)	0.767[b]
Regular exercise within past 3 months, yes (%)	37 (36.27)	1,197 (38.75)	0.612[b]
Family history of depression, yes (%)	17 (16.67)	179 (5.79)	<0.001[b]

BMI, body mass index; NTD, New Taiwan dollar; SD, standard deviation.
[a]Wilcoxon rank-sum test for significant differences ($P < 0.05$) between depressive and non-depressive subjects.
[b]Chi-square test for significant differences ($P < 0.05$) between depressive and non-depressive subjects.

TABLE 2 Distributions of annual 24-h road traffic noise and fine particles.

Exposure Level	Mean ± SD	Median	Range	Q1, Q3	IQR
$L_{eq,24h}$ (dBA)	68.12 ± 3.74	69.26	57.39–72.71	66.69, 71.42	4.73
31.5 Hz (dB)	27.95 ± 1.43	27.90	25.38–31.59	26.86, 29.45	2.59
63 Hz (dB)	42.36 ± 3.19	43.08	29.39–54.65	41.41, 44.63	3.22
125 Hz (dB)	51.13 ± 3.09	51.50	37.92–57.32	49.15, 52.87	3.72
250 Hz (dB)	55.43 ± 3.49	56.17	44.13–61.33	53.08, 57.59	4.51
500 Hz (dB)	60.12 ± 3.08	60.86	50.43–65.46	58.26, 62.25	3.99
1,000 Hz (dB)	64.47 ±4.24	65.49	48.97–71.15	62.83, 68.00	5.17
2,000 Hz (dB)	62.22 ± 4.06	63.49	48.90–67.28	60.89, 65.70	4.81
4,000 Hz (dB)	57.64 ± 2.99	58.39	47.32–61.20	56.72, 59.58	2.86
8,000 Hz (dB)	56.20 ± 2.46	56.52	42.91–63.31	54.78, 58.04	3.26
$PM_{2.5}$ (μg/m^3)	32.39 ± 5.38	33.00	17.68–46.98	28.41, 36.60	8.19

dB, decibel; dBA, A-weighted decibel; IQR, Interquartile range; SD, Standard deviation.

4. Discussion

4.1. Main findings

This study found that exposure to 24-h road traffic noise was significantly associated with the prevalent risk of depression after adjusting for $PM_{2.5}$. Participants exposed to 24-h road traffic noise ≥71.4 dBA had a significant higher risk of depression than those exposed to <66.7 dBA, and an IQR (4.7 dBA) increase in full frequency was significantly associated with the prevalent depression. These findings are similar to those reported in past studies. A linear exposure-response relationship was found in road traffic noise with an OR of 1.17 (95% CI: 1.10–1.25) for 24-h continuous sound levels ≥70 dB (12). A German prospective cohort study pointed out that when compared with the ≤55 dBA category, the incidence of depressive symptoms was significantly higher than in those with an exposure >55 dBA (RR=1.29, 95% CI: 1.03–1.62) category after adjusting for traffic proximity (10). However, we observed a stronger association between 24-h road traffic noise exposure and depression compared with those findings after controlling for the confounders of $PM_{2.5}$. Exposure to one IQR (16.7 μg/m^3) of $PM_{2.5}$ was found to be associated with self-reported psychological distress (OR=1.09, 95% CI: 1.07–1.12), hypnotic and sedative use (OR=1.04, 95% CI: 1.00–1.09), and antidepressant treatments (OR=1.01, 95% CI: 1.00–1.03) after adjusting for road traffic noise (22). Therefore, both road traffic noise and $PM_{2.5}$ should be considered to estimate the unbiased impacts on mental health.

The possible biological mechanism of road traffic noise exposure in depression is that noise may activate the central nervous system of emotional processing as a threat to homeostasis (31). There are two

TABLE 3 Correlations between the annual 24 h road traffic noise and fine particles.

Exposure variables	$PM_{2.5}$ ($\mu g/m^3$)	
	r	*P*-value
$L_{eq,24h}$ (dBA)	0.34	<0.001
31.5 Hz (dB)	0.64	<0.001
63 Hz (dB)	0.59	<0.001
125 Hz (dB)	0.31	<0.001
250 Hz (dB)	0.17	<0.001
500 Hz (dB)	0.45	<0.001
1,000 Hz (dB)	0.29	<0.001
2,000 Hz (dB)	0.34	<0.001
4,000 Hz (dB)	0.53	<0.001
8,000 Hz (dB)	0.51	<0.001

dB, decibel; dBA, A-weighted decibel; r, Spearman correlation coefficient.

main allostatic regulatory systems for stress responses: the HPA axis and the sympathetic–adrenal–medullary axis (32). Chronic exposure to stress may affect the HPA axis to generate metabolic changes that pose the impaired immune function, diabetes, depressive symptoms, and cognitive disturbances (33). An animal experimental study showed that rats exposed to noise produced more free radicals, which might increase superoxide dismutase activity (34), consequently causing systemic inflammation and oxidative stress. These responses lead to the destruction of the nervous system and melancholic behaviors (35).

This is the first study to determine the association between the frequency spectrum of road traffic noise and the prevalence of depression. Residents exposed to mid-high frequencies of road traffic noise (i.e., 1,000 and 2,000 Hz) were significantly associated with an elevated risk of depression to present exposure-response trends. Another mechanism underlying the association between noise and depression is chronic physical illness. The prevalent depression was found to be higher among diabetic patients (20%) than among asthmatics (12%) and healthy individuals (4%) in a comparative study (36). Furthermore, the hypertensive and diabetic subjects had the higher prevalent depression than the general population in Peruvian (37). Mid-to-high-frequency noise exposure has an adverse effect on insulin control and leads to a rise in blood sugar, which may cause type 2 diabetes mellitus between 1,000 and 2,000 Hz (38). Besides the insulin control, noise exposure may cause inflammatory pathways and oxidative stress to drive the adverse health effects on brain (7). In addition, exposure to road traffic noise at 1,000 Hz has been found to have a significant and positive relationship with prevalent hypertension (16) that is a risk factor of stroke. Low-frequency noise at 10–250 Hz was found to be associated with annoyance (17, 18), but this study did not observe significant associations between prevalent depression and noise exposure at low-frequency components. These evidences indicate that people may have higher perception to noise at frequencies higher than 1,000 Hz. Therefore, it was inferred that exposure to frequency components of 1,000 and 2,000 Hz might affect the prevalence of depression in chronic diseases.

The present study did not show a significant association between $PM_{2.5}$ exposure and prevalent depression. In addition, further analyses of interaction effects between noise frequency components and $PM_{2.5}$ did not find any significant interactions. However, a cross-sectional study had observed the association between one IRQ increase in $PM_{2.5}$ and prevalence of psychological distress after adjusting for road traffic noise (22). The possible reasons for this inconsistence may be that psychological distress is a symptom with sentiment which may change over a short period of time (39).

4.2. Strengths and limitations

The major advantage in this study was the application of predictive models with the high predictive ability (adjusted R^2: 0.7–0.8) for both 24-h road traffic noise and their frequency components (25), and a moderate predictive ability (adjusted R^2: 0.5) for $PM_{2.5}$ (26). These models provide better exposure assessments for residents living in Taichung, Taiwan than traditional approaches used in previous studies by either the closest monitoring station (40) or inverse distance relationship (41) to investigate the associations between road traffic noise and air pollutants with adverse health effects. Another advantage is the application of the Taiwan Biobank database, which is systematic sampling data that can represent the general population in Taichung. Furthermore, the present study is the first to determine the association between noise spectrum and prevalence of depression.

However, the present study has some limitations. First, we could not build a causality between depression and noise exposure because of the inherent restriction of temporality in the cross-sectional study design. Second, depression was assessed using one question in the survey, and no medical records were available to confirm the time of diagnosis and remission. It would be better to use a standardized scale for assessing depressive symptoms because many people with depression will never be diagnosed by a physician as they will not attend to the doctor. Third, the land-use regression method was a space-time geostatistical algorithm based on resident address, which limited the precise measurements of individual exposure levels. The non-differential misclassification of exposure for all subjects might bias the effect estimate to generate the null value of 1.0, but we still observed the significant associations between exposure to road traffic noise and specific noise spectrum and the prevalent depression. Fourth, temperature was not adjusted in our model, although it was reported to be associated with an increased risk of incident depression (RR=1.31, 95% CI: 1.09–1.56) at a daily mean temperature of 16.4°C (42). Fifth, the lack of data on sleep quality information might lead to overestimation of noise exposure effects on depression. Noise is a strong risk factor for depression because it has been found to cause poor sleep quality (43). Finally, work-related job stress, which was a confounder to be adjusted for in the data analysis, was not measured in this study (44).

5. Conclusions

In summary, we found a significant association between 24-h road traffic noise exposure and an increased risk of prevalent depression. The mid-to-high-frequency components at 1,000 and 2,000 Hz were found to be related to the prevalent depression, providing a possible link between noise exposure and mental

TABLE 4 Associations between one interquartile-range increase in annual 24-h road traffic noise and prevalent depression.

Variables	Model 1		Model 2		Model 3		Model 4	
	Crude OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Noise level								
$L_{eq,24h}$ (4.7 dBA)	1.32 (0.99–1.75)	0.056	1.69 (1.10–2.58)	0.016	1.61 (1.05–2.48)	0.029	1.62 (1.03–2.55)	0.037
Frequency components								
31.5 Hz (2.6 dB)	1.09 (0.76–1.56)	0.644	1.52 (0.92–2.50)	0.099	1.34 (0.80–2.25)	0.268	1.36 (0.70–2.62)	0.363
63 Hz (3.2 dB)	0.99 (0.81–1.20)	0.911	0.99 (0.76–1.28)	0.931	0.94 (0.73–1.22)	0.639	0.87 (0.66–1.16)	0.344
125 Hz (3.7 dB)	1.10 (0.86–1.40)	0.466	1.09 (0.79–1.50)	0.620	1.04 (0.75–1.43)	0.827	1.01 (0.72–1.41)	0.951
250 Hz (4.5 dB)	1.23 (0.93–1.63)	0.141	1.54 (1.03–2.32)	0.036	1.49 (0.99–2.24)	0.059	1.47 (0.98–2.22)	0.066
500 Hz (4.0 dB)	1.22 (0.92–1.61)	0.170	1.52 (1.02–2.29)	0.042	1.48 (0.98–2.24)	0.065	1.48 (0.94–2.32)	0.088
1,000 Hz (5.2 dB)	1.34 (1.02–1.75)	0.036	1.64 (1.11–2.42)	0.013	1.58 (1.06–2.35)	0.025	1.58 (1.05–2.37)	0.029
2,000 Hz (4.8 dB)	1.31 (1.00–1.71)	0.049	1.65 (1.10–2.47)	0.016	1.58 (1.05–2.38)	0.029	1.58 (1.03–2.43)	0.036
4,000 Hz (2.9 dB)	1.21 (0.96–1.51)	0.101	1.43 (1.01–2.02)	0.043	1.38 (0.97–1.94)	0.071	1.38 (0.94–2.01)	0.099
8,000 Hz (3.3 dB)	1.04 (0.79–1.37)	0.762	1.05 (0.73–1.51)	0.780	1.00 (0.70–1.44)	0.989	0.96 (0.66–1.39)	0.823

CI, Confidence interval; dB, decibel; dBA, A-weighted decibel; OR, Odds ratio.

Model 1, single exposure variable; Model 2, Model 1 with adjustment for regular exercise within 3 months, cigarette smoking, and monthly self-income; Model 3, Model 2 with adjustment for age, sex, BMI, drinking, married vs. unmarried and married vs. divorced, and family history; Model 4, Model 3 with adjustment for $PM_{2.5}$.

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TABLE 5 Associations between different 24-h road traffic noise exposure groups (by quartile) and prevalent depression.

Variables	Model 3		Model 4		Trend
	Adjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value	*P*-value
Noise level, $L_{eq,24h}$					
66.7–69.3 vs. < 66.7 dBA	1.03 (0.42–2.54)	0.949	1.06 (0.42–2.71)	0.902	**0.009**
69.3–71.4 vs. < 66.7 dBA	1.33 (0.58–3.05)	0.503	1.37 (0.57–3.26)	0.479	
≥71.4 vs. < 66.7 dBA	2.55 (1.20–5.42)	0.015	**2.65 (1.16–6.05)**	**0.021**	
Frequency components					
31.5 Hz, 26.9–27.9 vs. <26.9 dB	0.82 (0.36–1.91)	0.653	0.84 (0.35–2.02)	0.688	0.201
31.5 Hz, 27.9–29.5 vs. <26.9 dB	0.91 (0.41–2.02)	0.822	0.93 (0.39–2.23)	0.870	
31.5 Hz, ≥29.5 vs. <26.9 dB	1.56 (0.74–3.32)	0.247	1.61 (0.62–4.17)	0.329	
63 Hz, 41.4–43.1 vs. <41.4 dB	0.52 (0.23–1.21)	0.128	0.46 (0.18–1.17)	0.102	0.278
63 Hz, 43.1–44.6 vs. <41.4 dB	0.45 (0.17–1.17)	0.100	0.39 (0.14–1.12)	0.080	
63 Hz, ≥44.6 vs. <41.4 dB	1.30 (0.67–2.52)	0.433	1.10 (0.46–2.59)	0.833	
125 Hz, 49.2–51.5 vs. <49.2 dB	0.62 (0.27–1.44)	0.265	0.46 (0.18–1.15)	0.096	0.376
125 Hz, 51.5–52.9 vs. <49.2 dB	0.79 (0.36–1.71)	0.547	0.51 (0.20–1.31)	0.162	
125 Hz, ≥52.9 vs. <49.2 dB	1.29 (0.65–2.57)	0.465	1.07 (0.51–2.21)	0.864	
250 Hz, 53.1–56.2 vs. <53.1 dB	1.22 (0.52–2.84)	0.644	1.19 (0.49–2.87)	0.699	0.141
250 Hz, 56.2–57.6 vs. <53.1 dB	1.64 (0.75–3.58)	0.216	1.57 (0.66–3.75)	0.307	
250 Hz, ≥57.6 vs. <53.1 dB	1.70 (0.76–3.77)	0.194	1.67 (0.74–3.76)	0.215	
500 Hz, 58.3–60.9 vs. <58.3 dB	1.21 (0.50–2.93)	0.666	1.26 (0.51–3.08)	0.615	0.059
500 Hz, 60.9–62.3 vs. <58.3 dB	2.20 (1.01–4.79)	0.047	2.39 (1.01–5.66)	0.047	
500 Hz, ≥62.3 vs. <58.3 dB	1.84 (0.78–4.34)	0.162	2.01 (0.79–5.16)	0.144	
1,000 Hz, 62.7–65.5 vs. <62.7 dB	1.16 (0.48–2.79)	0.749	1.14 (0.45–2.87)	0.780	**0.015**
1,000 Hz, 65.5–68.0 vs. <62.7 dB	1.32 (0.56–3.10)	0.521	1.30 (0.53–3.19)	0.561	
1,000 Hz, ≥68.0 vs. <62.7 dB	2.51 (1.14–5.50)	0.022	**2.47 (1.07–5.70)**	**0.033**	
2,000 Hz, 60.7–63.5 vs. <60.7 dB	0.96 (0.39–2.37)	0.936	0.98 (0.38–2.51)	0.963	**0.009**
2,000 Hz, 63.5–65.7 vs. <60.7 dB	1.29 (0.55–2.98)	0.559	1.31 (0.54–3.18)	0.557	
2,000 Hz, ≥65.7 vs. <60.7 dB	2.55 (1.16–5.59)	0.020	**2.60 (1.10–6.12)**	**0.029**	
4,000 Hz, 56.7–58.4 vs. <56.7 dB	0.95 (0.41–2.20)	0.899	0.99 (0.42–2.38)	0.989	0.103
4,000 Hz, 58.4–59.6 vs. <56.7 dB	1.09 (0.49–2.42)	0.836	1.17 (0.50–2.76)	0.719	
4,000 Hz, ≥59.6 vs. <56.7 dB	1.82 (0.85–3.88)	0.123	2.09 (0.80–5.50)	0.134	
8,000 Hz, 54.8–56.5 vs. <54.8 dB	0.58 (0.24–1.39)	0.219	0.53 (0.21–1.37)	0.189	0.202
8,000 Hz, 56.5–58.0 vs. <54.8 dB	0.57 (0.25–1.33)	0.194	0.53 (0.22–1.31)	0.169	
8,000 Hz, ≥58.0 vs. <54.8 dB	1.50 (0.77–2.94)	0.233	1.35 (0.60–3.04)	0.475	

CI, Confidence interval; dB, decibel; dBA, A-weighted decibel; OR, Odds ratio.
Model 3, adjustment for age, sex, BMI, monthly self-income, married vs. unmarried and married vs. divorced, cigarette smoking, alcohol drinking, regular exercise within 3 months, and family history; Model 4, Model 3 with adjustment for $PM_{2.5}$ levels. The bold values indicate the significant results ($p < 0.05$) in regression models.

health. We recommend that future studies are performed using a longitudinal design to confirm these findings.

Data availability statement

The dataset of Taiwan Biobank is available for registration and requirement. Requests to access these datasets should be directed to Taiwan Biobank, biobank@gate.sinica.edu.tw.

Ethics statement

The studies involving human participants were reviewed and approved by Central Regional Research Ethics Committee of China Medical University, Taichung, Taiwan (protocol number: CRREC-108–006). The patients/participants provided their written informed consent to participate in this study.

Author contributions

J-YL and T-YC conceived and designed the study and performed data analyses. J-YL, W-JC, C-FW, and T-YC collected and assembled the data. J-YL, W-JC, and T-YC wrote the manuscript. C-FW made critical revision of the manuscript for key intellectual content. T-YC handled funding and supervision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Perceived social cohesion and depressive symptoms among internal migrants in China: The mediating role of social adaptation

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Background: Internal migrants are exposed to higher risks of depressive symptoms due to migration-related stress. It has been recognized that perceived neighborhood social cohesion has direct and indirect associations with depressive symptoms. However, the pathway from perceived social cohesion to internal migrants' depressive symptoms was less discussed.

Objectives: To assess mental health disparities among internal migrants. To investigate the association between social cohesion and depressive symptoms among urban-to-urban and rural-to-urban migrants and to examine the mediating role of social adaptation.

Methods: Data from the "2017 Urbanization and New Migrant Survey" was used, including 2,584 internal migrants age 18–65 from 10 cities in China. Social cohesion was measured by a six-item modified Community-level Cohesion Scale. Depressive symptoms was measured using the Center for Epidemiological Studies Depression Scale, and social adaptation was assessed by a single-item question of migrants' adaptation to local life. Multivariate linear regression models were used to examine the association between social cohesion and depressive symptoms. Baron and Kenny's mediation tests were conducted to examine the mediating role of social adaptation on the association. All analyses were adjusted using sampling weights to account for this survey's sampling design.

Results: Rural-to-urban migrants were found to have more clinically significant depressive symptoms, lower perceived social cohesion, and fair or low social adaptation than urban-to-urban migrants (all $p < 0.001$). Being rural-to-urban migrants as compared with urban-to-urban migrants [Odds Ratio (OR) = 1.46, 95% Confidence Interval (CI) = 1.456, 1.461, $p < 0.001$], had lower perceived social cohesion (OR = 1.46, 95% CI = 1.458, 1.463, $p < 0.001$), and poorer social adaptation (OR = 1.94, 95% CI = 1.932, 1.941, $p < 0.001$), are associated with higher odds of having clinically significant depressive symptoms. Social adaptation partially mediated the association between social cohesion and depressive symptoms by explaining 15.39% of its effect for urban-to-urban migrants and 18.97% for rural-to-urban migrants.

Conclusions: Findings from this study reveal mental health inequalities among internal migrants and demonstrate the importance of social adaption on the association between social cohesion and depressive symptoms. Social strategies and public policies are needed to build a more cohesive community that serves both local residents and internal migrants, especially rural-to-urban migrants.

KEYWORDS

social cohesion, social adaptation, depression, migration, mental health disparities

Introduction

Depressive symptoms are common mental health problems among migrants in many countries. This issue could be exacerbated due to an increase in the migrant population around the world (1). Internal migrants are individuals who migrate between regions within one country (2). Due to China's economic development since 1978, internal migrants have increased dramatically. Internal migrants reached 244 million in 2017, accounting for more than 17.5% of the total population (3). For migrants, depressive symptoms are especially associated with their intention to settle in the host place (4). However, the mental health status of internal migrants did not receive much attention (5, 6).

Increasing evidence suggests that migrants experience higher levels of depressive symptoms than native-born residents (7–10) because of migration-related changes, such as separation from family, reducing size in social support, and weakened social ties (11). In China, migration has been regarded as a stressful process (10, 12). For migrants, due to the housing registration system (i.e., *Hukou*) that limits their access to employment, education, housing, and health insurance (13, 14), they are more likely to be exposed to social stress and social exclusion (6, 11, 12, 15) that may lead to a higher level of depressive symptoms. There are two major internal migration patterns in China: one is from rural-to-urban migration and the other from urban-to-urban migration (16). However, most previously studies that examined mental health status were only focused on rural-to-urban migrants (5, 11, 17, 18).

In addition, it has long been recognized that individual and family level social factors, such as family socioeconomic status, social capital, and social support, have direct relationships with depressive symptoms (19–24), while little attention has been paid on the role of social cohesion, as a community-level social factor that is associated with depressive symptoms among internal migrants. Social cohesion indicates the inclusion and integration of a community (25, 26). As an important environmental factor, social cohesion is related to individuals' psychological wellbeing (27, 28). In a migrant community, social cohesion has an impact on internal migrants' positive interactions including obtaining social support and help, or negative interactions such as suffering from social stress and/or exclusion from native-born residents. However, little attention has been paid to the association of social cohesion, as a community-level social factor, with depressive symptoms among internal migrants in China.

The rapid increase of the migration population, intertwined with dramatic social transition, suggests that Chinese society has reached a critical stage in mental health care challenges. Nevertheless, little is known about how social environmental context, beyond intra-personal factors, affects depressive symptoms among internal migrants in China. To address these knowledge gaps, this study aims to investigate the association between social cohesion and depressive symptoms among urban-to-urban and rural-to-urban migrants and to examine the mediating role of social adaptation, using the data drawn from the "2017 Urbanization and New Migrant Survey," a large-scale sample with 2,584 internal migrants from 10 cities in China. Gaining a better understanding of the pathways would provide a better knowledge on community-level social factors that are associated with depressive symptoms and help develop social strategies and public policies in addressing mental health issues among migrant population.

Literature review

Social inequalities: Disparities in depressive symptoms within migrants

When studying the migrant-related health disparities, scholars often use a native-born population in the host society as the reference group. Most of the studies demonstrated that migrants had poorer mental health, e.g., depressive symptoms, than native-born residents (6, 11, 29, 30). Depressive symptoms may lead to a series of complications that affect individual's quality of life and cause other critical health issues such as suicide, frailty, functional disability, and mortality (31–33). For migrants (including both international and internal migrants), depressive symptoms are also associated with their intention to settle down in the host place (4).

However, most studies on health outcomes in China only focused on the rural-to-urban migrants (6, 11, 17, 18). These studies suggest that there are significant mental health disparities within migrants. Furthermore, more information about migration status, e.g., the housing registration status of migrants, and reasons for migration, should be considered when examining the mental health disparities among migrants. In China, the most important characteristic that distinguishes the patterns of migration from those in other countries is the housing registration system (*Hukou* system) (13, 34). Since *Hukou* is linked with entitlement and benefits for individuals, whether migrants come from urban or rural is an indicator for their education background, financial status, and social support (13, 34–36), which may result in different mental health outcomes, such as depressive symptoms. To assess disparities in depressive symptoms among migrants, we proposed the following hypothesis:

> Hypothesis 1: Rural-to-urban migrants are more likely to have a higher level of depressive symptoms than urban-to-urban migrants.

Social cohesion in reducing depressive symptoms

There is no doubt that environmental context plays a crucial role in shaping psychological wellbeing (27, 37, 38). When investigating risk and protective factors for depressive symptoms of migrants, it is likely that community-level factors are at play.

It is well-recognized that individual and neighborhood-level factors, such as neighborhood socioeconomic status, social capital, and social support, have strong associations with residents' depressive symptoms (19–22, 37–43). A related concept of particular importance to the migrant community is social cohesion (27, 44). Social cohesion refers to communal bonds characterized by altruism, reciprocity, and shared norms and values (27). It generates mutual trust and support, collective efficacy, and a sense of belonging, which are all conducive to improved mental health (27, 45). Previous studies show that social cohesion was defined as a neighborhood-level factor, and lower neighborhood social cohesion was linked to a variably of health outcomes, such as depression and mortality (46–52).

Neighborhood social cohesion is the network of relationships, shared values, and norms of residents in a neighborhood and it shares some similarities to an individual's social network (53). Social

cohesion, however, exists in a larger field. It accounts for value systems, degree of social interaction, and considers the cohesion of a broader community rather than cohesion within a neighborhood or a small group of individuals. However, little attention has been paid to the association of social cohesion, as a community-level social factor, with depressive symptoms among internal migrants in China. In a migrant community, social cohesion refers to the quality of social interactions which is closely related to individuals' mental health status (11, 20, 22, 41, 54). In a more cohesive community, migrants may feel a stronger sense of inclusion. Social cohesion has an impact on internal migrants' positive interactions including obtaining social support and help, or negative interactions such as suffering from social stress and/or exclusion from native-born residents. In a community where native-born residents and migrants trust each other, they will have more social connections and interactions. For migrants, the trust they have built will make it easier for them to establish new social ties and social networks that are important to adapt to a new life and maintain a good psychological status (20, 21, 42). In addition, a higher level of social cohesion would lead to less social stress or social exclusion, which may result in fewer depressive symptoms (6, 11, 12). Furthermore, in a well-integrated community, native-born residents and migrants are more likely to provide mutual social support, which is a protective factor against depressive symptoms (22, 41). Even if some migrants suffer from depressive symptoms, they are more likely to be able to receive timely assistance in a more cohesive community. To investigate the associations between social cohesion and depressive symptoms of both urban-to-urban and rural-to-urban migrants, here is the second hypothesis:

> Hypothesis 2: A lower level of perceived social cohesion is associated with more depressive symptoms among both urban-to-urban and rural-to-urban migrants.

Social adaptation: Pathways from social cohesion to depressive symptoms

Although recent studies have shown the correlation between social cohesion and health outcomes (49, 50, 52, 55, 56), limited studies have been conducted to examine the mediating role of social adaptation on the association between social cohesion and migrants' mental health. Increasing attention has been paid to improve social adaptation as an effort to improve individual's mental health (57, 58). Social adaptation concerns the interactions between an individual and the environment. It refers to the performance in the activities of daily intercultural living (59) and involves the intercultural competence with emphasis on behavioral domains. As an important indicator of migrants' integration into the host community, social adaptation would mediate the pathways from social cohesion to depressive symptoms. Individual's allostatic load would be lower in a highly cohesive community where internal migrants have more positive interactions with local residents and a higher sense of being trusted and belonging, Individuals are more likely to "doing well" in the activities of daily intercultural living in the host city (59). Additionally, "doing well" in social adaptation may help buffer the effects of social stress and social exclusion they may face in the migration process (6, 11, 12); thus, avoiding the occurrence of psychological disorders. Therefore, no such studies have been conducted to examine whether social adaptation is a factor that could mediate between social cohesion and depressive symptoms. Thus, we propose the following hypothesis:

> Hypothesis 3: Social adaptation mediates the association between social cohesion and depressive symptoms for both urban-to-urban and rural-to-urban migrants.

Methods

Data source and study sample

Data were drawn from the "2017 Urbanization and New Migrant Survey," a cross-sectional survey focusing on policy issues such as population migration, social mobility, and social integration in Chinese adults. A multi-stage stratified sampling strategy was used, and data were collected from 10 cities in China, including economically developed cities (GDP per capita of is more than 100,000 RMB), such as Zhengzhou, Tianjin, Xiamen, Guangzhou, and Changsha, and less developed ones (GDP per capita of is <100,000 RMB), including Harbin, Changchun, Yanji, Shenyang, and Anshan. Data were collected during in-home interviews by well-trained interviewers. Inclusion criteria for participation were: (1) full-time residence in this city >6 months in the past year; (2) aged 18–65 years; and (3) capable of communicating answers to interview questions and giving consent.

A sample of 2,752 adult internal migrants (i.e., the movement of people between usual residences within national states) were drawn from the survey data. After excluding 168 adults with missing values, the final analytical sample consisted of 2,584 internal migrants. Among them, 1,152 reported living in another urban area before moving to their current locations, defined as urban-to-urban migrants, and 1,432 reported living in a rural area before moving to their current locations, defined as rural-to-urban migrants.

Measures

Dependent variables: Depressive symptoms

Depressive symptoms were measured using the original 20-item version of the Center for Epidemiological Studies Depression Scale (CES-D), a widely used screening measure for depressive symptoms (60). The CES-D assesses how often a person has experienced symptoms of depression, such as restless sleep, poor appetite, and feeling lonely over the past week. Each scale item is scored from 0 to 3, with a higher score representing greater depressive symptom severity. The potential range of the scale is 0–60. A cut-off score of 16 or higher is generally used to determine clinically significant depressive symptoms (61). The Cronbach's alpha for the total scale was 0.873, indicating favorable internal-consistency.

Independent variables: Social cohesion

The concept of perceived social cohesion in this study focuses on native-born residents' intergroup relationships with internal migrants. It refers to whether internal migrants could perceive a high or low sense of being welcomed and trusted by local residents or belonging to the community (62). With reference to the neighborhood-level cohesion scale (63–65), we generated a summary

variable based on six questions, including "How much do you think native-born people are willing to (1) work with you; (2) talk with you; (3) be your neighbors; (4) make friends with you; (5) be your relatives; (6) manage the community together with you?" Each item was scored 1–5, 1 = very unwilling to, 2 = unwilling to, 3 = fair, 4 = willing to, and 5 = very willing to, with lower values representing lower perceived social cohesion. The potential range of the scale is 0–30. The six items showed good internal consistency in this study (Cronbach's $\alpha = 0.929$). Considering that the median score on the social cohesion scale was 24, we then dichotomized the variable, with scores below 24 indicating a low perception of social cohesion.

Mediating variables: Social adaptation

Social adaptation was assessed based on the single-item question: "How much do you think you have adapted to local life?" The five-point response to this question—very poor, poor, fair, good, and very good—was then dichotomized into participants who reported fair or poor social adaptation vs. all else. Approximately 13% of the sample was categorized into the fair or poor category. We chose the fair or poor cut-off point because this is a qualitatively different group of migrants than those who are "doing well" and reporting good, or very good social adaptation (59).

Control variables

We included a set of confounding variables associated with depressive symptoms (7–10). Specifically, we controlled for: (i) socio-demographic characteristics, including gender (1 = female, 0 = male), age (in years), marital status (1 = married or with a partner, 0 = single or without a partner), education (years of schooling), and income (log-transformed); (ii) health behaviors, including smoking (1 = current smoker, 0 = non-smoker), alcohol consumption (1 = less than once a month, 2 = one to three times a month, 3 = one or two times a week, 4 = three to four times a week, and 5 = almost every day), and physical activity (1 = never, 2 = once a month, 3 = two or three times a month, 4 = two or three times a week, and 5 = almost every day); (iii) health status measured by self-reported physician-diagnosed chronic diseases (yes or no), including type 2 diabetes, hypertension, and heart disease. Additionally, we controlled for migration characteristics, including reasons for migration, migration time (in years), and city of residence. Reasons for migration were dichotomized into voluntary migration, which includes training or career opportunities (i.e., labor migration, occupation mobility, training and learning, and business investment), and involuntary migration for marriage or family reunion. Time since migration (in years) indicated how long migrants lived in the hosting city. The city of residence was dichotomized into more developed or less developed, depending on whether the GDP per capita of the hosting city is more than 100,000 RMB (equivalent to 14,286 US dollars).

Analytic strategy

We used Stata 15.0 for all statistical analysis (66). We used descriptive statistics to characterize the analytical sample separately for urban-to-urban and rural-to-urban migrants. To assess the disparities between groups, we conducted ANOVA tests for continuous variables and Chi-squared tests for categorical variables

The bivariate logit models were used to examine whether there were significant differences in depressive symptoms between different groups. The multivariate linear regression models were used to examine the associations between social cohesion and depressive symptoms for both groups. Testing for mediation presumes a causal chain of events. The analyses cannot actually prove this causality, but they can show whether the data are in alignment with the proposed chain of events. In our analyses, we followed the procedure for establishing mediation proposed by Baron and Kenny (67). Adjusting for all covariates, we examined the mediating role of social adaptation on the association between social cohesion and depressive symptoms (67). Sobel and Goodman's methods were adapted to test the indirect effects of the mediating variables (68, 69).

Weighting

A multi-stage stratified sampling strategy was used, and the sampling process involved four stages: city, neighborhood, household, and individual. Ten cities were selected from seven provinces in China. At the city level, 20 neighborhoods were randomly selected from each city. At the neighborhood level, 25 households were selected from a housing registration database obtained from each neighborhood community. One individual was selected from each selected household. In this survey, the quota for migrants and non-migrants was designed to be close to 1:1. The "2017 Urbanization and New Migrant Survey" has individual-level sampling weights that take the complex sampling design into consideration. We defined the city as SU ($n = 10$), and the neighborhood as strata ($n = 20$). All analyses presented in Tables 1–4 were adjusted for sample weights (70).

Results

Descriptive statistics

Descriptive characteristics of the final weighted analytical sample are presented by migration status in Table 1. Rural-to-urban migrants were found to have more clinically significant depressive symptoms than urban-to-urban migrants (32.86 vs. 25.12%, $p < 0.001$). Approximately 43.87% of rural-to-urban migrants reported low social cohesion compared to 31.96% of urban-to-urban migrants. Approximately 16.46% of rural-to-urban migrants reported fair or low social adaptation compared to 7.99% of urban-to-urban migrants. Moreover, rural-to-urban migrants were less educated than urban-to-urban migrants. They tended to stay in the hosting city for a shorter duration (12.26 vs. 15.99 years, $p < 0.001$).

Prevalence of depressive symptoms by migration status, social cohesion, and social adaptation

Weighted prevalence of depressive symptoms by migration status, social cohesion, social adaptation and covariates are presented in Table 2. Results showed that being rural-to-urban migrants as compared with urban-to-urban migrants [Odds Ratio (OR) = 1.46, 95% Confidence Interval (CI) = 1.456, 1.461, $p < 0.001$], had lower perceived social cohesion (OR = 1.46, 95% CI = 1.458, 1.463, $p < 0.001$), and poorer social adaptation (OR = 1.94, 95% CI = 1.932,

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TABLE 1 Descriptive statistics by migration status (weighted).

	Total	Migration status		*p*-value
		Urban-to-urban	Rural-to-urban	
	N = 2,584	*N* = 1,227	*N* = 1,357	
	%/mean (SD)	%/mean (SD)	%/mean (SD)	
Depressive symptoms (CES-D score)				<0.001
No (scored 1–15)	70.82	74.88	67.14	
Yes (scored 16–60)	29.18	25.12	32.86	
Social cohesion				<0.001
Moderate-high	61.79	68.04	56.13	
Low	38.21	31.96	43.87	
Social adaptation				<0.001
Good	87.57	92.01	83.54	
Fair or poor	12.43	7.99	16.46	
Gender				<0.001
Male	45.20	42.68	47.48	
Female	54.80	57.32	52.52	
Age (in years)	41.58 (13.35)	43.48 (13.85)	39.86 (12.64)	<0.001
Marital status				<0.001
Single or without a partner	23.61	26.12	21.33	
Married or with a partner	76.39	73.88	78.67	
Education (years of schooling)				<0.001
0 (illiterate)	1.63	0.38	2.76	
6 (elementary school)	6.53	1.57	11.02	
9 (middle school)	21.62	14.93	27.68	
12 (high/vocational school)	27.61	29.06	26.30	
15 (3 years college)	17.05	20.79	13.67	
16 (a bachelor' degree)	19.14	25.34	13.54	
19 (a master's degree or more)	6.41	7.94	5.03	
Income (log-transformed)	11.48 (1.86)	11.43 (1.80)	11.52 (1.91)	<0.001
Smoking				<0.001
Non-smoker	78.34	78.79	77.93	
Current smoker	21.66	21.21	22.07	
Alcohol consumption				<0.001
Less than once a month	76.22	77.64	74.93	
One to three times a month	8.64	8.56	8.72	
One to two times a week	7.34	6.28	8.30	
Three to four times a week	3.90	4.13	3.70	
Almost every day	3.90	3.38	4.36	
Physical activity				<0.001
Never	25.92	24.51	27.20	
Once a month	8.15	6.58	9.57	
Two or three times a month	18.15	19.53	16.89	
Two or three times a week	22.77	23.11	22.46	
Almost every day	25.02	26.28	23.88	

(Continued)

TABLE 1 (Continued)

	Total	Migration status		*p*-value
		Urban-to-urban	Rural-to-urban	
	N = 2,584	*N* = 1,227	*N* = 1,357	
	%/mean (SD)	%/mean (SD)	%/mean (SD)	
Diabetes				<0.001
No	96.85	95.73	97.87	
Yes	3.15	4.27	2.13	
Hypertension				<0.001
No	90.70	88.23	92.93	
Yes	9.30	11.77	7.07	
Heart diseases				<0.001
No	96.40	95.28	97.41	
Yes	3.60	4.72	2.59	
Reasons for migration				<0.001
Voluntary migration	62.58	50.03	73.94	
Involuntary migration	37.42	49.97	26.06	
Time since migration (in years)	14.03 (12.24)	15.99 (13.60)	12.26 (10.56)	<0.001
City of residence				<0.001
Less developed	30.78	31.14	30.45	
More developed	69.22	68.86	69.55	

Source. 2017 Urbanization and New Migrant Survey.
Comparisons between groups were done using Chi-squared tests for categorical variables and ANOVA tests for continuous variables.
CES-D, Center for Epidemiological Studies Depression Scale; SD, Standard Deviation.

1.941, $p < 0.001$), are associated with higher odds of having clinically significant depressive symptoms. Moreover, being married or with a partner (OR = 0.68, 95% CI = 0.679,0.682, $p < 0.001$) are associated with lower odds of having clinically significant depressive symptoms. Self-reported physician-diagnosed type 2 diabetes (OR = 1.71, 95% CI = 1.707,1.723, $p < 0.001$) and heart diseases (OR = 1.18, 95% CI = 1.172,1.183, $p < 0.001$) are associated with higher odds of having clinically significant depressive symptoms.

Associations between social cohesion and social adaptation

As shown in Table 3, fair or poor social adaptation was associated with a higher odd of migrants with a low perceived social cohesion for both urban-to-urban migrants (OR = 2.91, 95% CI = 2.89, 2.92, $p < 0.001$) and rural-to-urban migrants (OR = 4.12, 95% CI = 4.11, 4.13, $p < 0.001$). After adjustment for all covariates, the odds ratio reduced to 2.69 (95% CI = 2.67, 2.70, $p < 0.001$) for urban-to-urban migrants and 3.66 (95% CI = 3.65, 3.67, $p < 0.001$) for rural-to-urban migrants.

Associations between social cohesion and depressive symptoms

Table 4 shows the associations between social cohesion and depressive symptoms. As shown in Model 1, migrants with a low perceived social cohesion had a higher CES-D score for urban-to-urban migrants [$\beta = 1.17$, Standard Error (SE) = 0.005, $p < 0.001$] and rural-to-urban migrants ($\beta = 1.81$, SE = 0.004, $p < 0.001$) compared to those with moderate-high social cohesion. As shown in Model 2, the addition of covariates reduced the β-coefficient for low social cohesion to 0.78 (SE = 0.005, $p < 0.001$) for urban-to-urban migrants and 1.74 (SE = 0.004, $p < 0.001$) for rural-to-urban migrants. Moreover, the addition of social adaptation to Model 3 further reduced the β-coefficient for low social cohesion to 0.66 (SE = 0.005, $p < 0.001$) for urban-to-urban migrants and 1.41 (SE = 0.004, $p < 0.001$) for rural-to-urban migrants, and the associations remained significant.

Formal mediation analysis was conducted to examine the mediating role of social adaptation on the associations between social cohesion and depressive symptoms in both groups. The Sobel mediation tests were significant for both groups at the $p = 0.001$ level. Social adaptation partially mediated the association between social cohesion and depressive symptoms by explaining 15.39% of its effect for urban-to-urban migrants and 18.97% of its effect for rural-to-urban migrants.

Discussion

Using data from the "2017 Urbanization and New Migrant Survey," we investigated the association between social cohesion

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TABLE 2 Presence of depressive symptoms by migration status, social cohesion, social adaptation, and covariates (weighted).

	N	Presence of depressive symptoms (%)	OR	95% CI	*p*-value
Total	2,584	29.18			
Migration status					
Urban-to-urban migrants	1,227	25.12	Ref		
Rural-to-urban migrants	1,357	32.86	1.46	1.456–1.461	<0.001
Social cohesion					
Moderate-high	1,597	26.15	Ref		
Low	987	34.09	1.46	1.458–1.463	<0.001
Social adaptation					
Good	2,263	27.34	Ref		
Fair or poor	321	42.16	1.94	1.932–1.941	<0.001
Gender					
Male	1,168	28.34	Ref		
Female	1,416	29.89	1.08	1.076–1.080	<0.001
Age (in years)					
18–65	2,584	-	0.98	0.984–0.984	<0.001
Marital status					
Single or without a partner	610	35.49	Ref		
Married or with a partner	1,974	27.24	0.68	0.679–0.682	<0.001
Education (years of schooling)					
0 (illiterate)	42	27.76	Ref		
6 (elementary school)	168	30.87	1.16	1.154–1.171	<0.001
9 (middle school)	559	32.64	1.26	1.252–1.270	<0.001
12 (high/vocational school)	713	27.37	0.98	0.974–0.988	<0.001
15 (3 years college)	441	26.38	0.93	0.926–0.939	<0.001
16 (a bachelor' degree)	495	30.70	1.15	1.145–1.161	<0.001
19 (a master's degree or more)	166	26.90	0.96	0.951–0.965	<0.001
Income (log-transformed)					
0–16.11	2,584	-	1.03	1.033–1.034	<0.001
Smoking					
Nonsmoker	2,024	30.44	Ref		
Current smoker	560	24.64	0.75	0.745–0.749	<0.001
Alcohol consumption					
Less than once a month	1,969	29.47	Ref		
One to three times a month	223	30.06	1.03	1.026–1.032	<0.001
One to two times a week	190	25.66	0.83	0.823–0.829	<0.001
Three to four times a week	101	31.10	1.08	1.076–1.085	<0.001
Almost every day	101	26.47	0.86	0.858–0.866	<0.001
Physical activity					
Never	670	32.43	Ref		
Once a month	211	35.21	1.13	1.129–1.136	<0.001
Two or three times a month	469	32.21	0.99	0.987–0.992	<0.001
Two or three times a week	588	28.84	0.84	0.842–0.847	<0.001
Almost every day	646	21.98	0.59	0.585–0.588	<0.001

(Continued)

TABLE 2 (Continued)

	N	Presence of depressive symptoms (%)	OR	95% CI	*p*-value
Diabetes					
No	2,503	28.80	Ref		
Yes	81	40.96	1.71	1.707–1.723	<0.001
Hypertension					
No	2,344	29.39	Ref		
Yes	240	27.19	0.90	0.895–0.900	<0.001
Heart diseases					
No	2,491	29.06	Ref		
Yes	93	32.54	1.18	1.172–1.183	<0.001
Reasons for migration					
Voluntary migration	1,617	29.50	Ref		
Involuntary migration	967	28.66	0.96	0.958–0.962	<0.001
Time since migration (in years)					
0.5–63.5	2,584	-	0.99	0.986–0.986	<0.001
City of residence					
Less developed	795	30.00	Ref		
More developed	1,789	28.82	0.94	0.942–0.946	<0.001

Source. 2017 Urbanization and New Migrant Survey.
Comparisons between groups were done using bivariate logit regression.
OR, Odds Ratio; CI, Confidence Interval.

TABLE 3 Associations between social cohesion and social adaptation (weighted).

	Urban-to-urban migrants ($N = 1,227$)		Rural-to-urban migrants ($N = 1,357$)	
	OR	95% CI	OR	95% CI
Low social cohesion (unadjusted)	2.91***	2.89–2.92	4.12***	4.11–4.13
Low social cohesion (adjusted)	2.69***	2.67–2.70	3.66***	3.65–3.67

Source. 2017 Urbanization and New Migrant Survey.
Adjusted model controlled for socio-demographic characteristics, health behaviors, health status, and migration characteristics, including gender, age, marriage status, education, income, smoking, alcohol consumption, physical activity, diabetes, hypertension, heart disease, reasons for migration, migration time, and city of residence.
OR, Odds Ratio; CI, Confidence Interval.
*p < 0.05, **p < 0.01, ***p < 0.001.

and depressive symptoms among urban-to-urban and rural-to-urban migrants aged 18–65 in China and examined the mediating role of social adaptation. All three hypothesis were supported. The study findings demonstrated the significant mental health inequalities across urban-to-urban and rural-to-urban migrants. Also, we provided new knowledge to the field by identifying the protective role of social cohesion, as an important community-level factor, on depressive symptoms of migrants. Furthermore, this study identified the mediating role of social adaptation on the association between social cohesion and depressive symptoms. Our study has provided a scientific foundation for developing policy and research agenda to improve the mental health of migrants in China.

Mental health care challenges: Disparities in depressive symptoms within migrants

Our findings that rural-to-urban migrants had a higher prevalence of depressive symptoms than urban-to-urban migrants confirmed the mental health inequalities within migrants. Whether they migrated from urban or rural may have implications for their housing registration status (*Hukou*), educational background, financial status, social capital, and sense of wellbeing. All these factors are related not only to the challenges they may face in the migration process but also to their abilities to overcome the challenges that could affect their probability of suffering from depressive symptoms.

The limited resources and opportunities due to their *Hukou* could partially explain rural-to-urban migrants' higher prevalence of depressive symptoms. Rural *Hukou* limits their access to both economic and social resources in the host city. In this situation, the social stress and social exclusion they experienced may have significant mental health implications (6, 10–12). Our results showed that a higher proportion of rural-to-urban migrants had less perceived social cohesion and fair or poor social adaptation than urban-to-urban migrants. Although China has gradually relaxed its policies on its *Hukou* system, it remains challenging for rural-to-urban migrants, especially those with low education, to settle permanently in the receiving city or are entitled to the same social benefits as urban residents (14, 35, 36). These inequalities could limit their opportunities for upward mobility and ultimately affect their mental health outcomes.

Our results also suggest that, among rural-to-urban migrants, involuntary migrated participants had higher depressive symptoms than those who voluntarily migrated. Several reasons may shed a

TABLE 4 Linear regression models for depressive symptoms (CES-D score; weighted).

		Model 1		Model 2		Model 3	
		β	SE	β	SE	β	SE
Urban-to-urban migrants ($N = 1,227$)	Low social cohesion	1.17***	0.005	0.78***	0.005	0.66***	0.005
	Fair or low social adaptation					1.55***	0.008
	Sobel test of mediation: $p = 0.001$						
	% Explained by the addition of social adaptation = 15.39%						
Rural-to-urban migrants ($N = 1,357$)	Low social cohesion	1.81***	0.004	1.74***	0.004	1.41***	0.004
	Fair or low social adaptation					1.94***	0.006
	Sobel test of mediation: $p = 0.001$						
	% Explained by the addition of social adaptation = 18.97%						

Source. 2017 Urbanization and New Migrant Survey.
Model 1 adjusted only for social cohesion. Model 2 added in adjustment of socio-demographic characteristics, health behaviors, health status, and migration characteristics, including gender, age, marriage status, education, income, smoking, alcohol consumption, physical activity, diabetes, hypertension, heart disease, reasons for migration, migration time, and city of residence. Model 3 added in the effects of social adaptation.
SE, Standard Error.
*p < 0.05, **p < 0.01, ***p < 0.001.

slight on the findings. For example, these involuntary migrants may have limited social connections because family members are likely to be the only social network they can interact with. In addition, involuntary migrants have limited access to formal financial support, social capital, and health insurance, all are considered protective factors for maintaining good mental health (19).

Social strategies: Building a higher cohesive community

Findings on the association between social cohesion and depressive symptoms are in line with previous studies which demonstrated that a higher level of neighborhood social cohesion is associated with better mental health outcomes (49, 50, 52, 55, 56).

Findings from linear regression models indicate that the level of depressive symptoms of rural-to-urban migrants is more dependent on social cohesion. It seems that social environmental context is even more important for rural-to-urban migrants' psychological wellbeing than for urban-to-urban migrants. In a host city, rural-to-urban migrants face much greater mental health risks than urban-to-urban migrants (6, 11, 17, 18); including (i) lack of urban *Hukou* that comes with a variety of economic and social resources (i.e., social security, unemployment insurance, and health insurance). (ii) Lack of sufficient level of education that could help them achieve a stable occupation and a higher socioeconomic position. (iii) Lack of sufficient social capital that is an important protective factor of psychological wellbeing. Although social capital appears to exist among rural-to-urban migrants, they have less-developed organizational social networks. Most of them rely on family members and friends from hometowns as primary personal networks (71). Thus, we speculate that they are more in need of support and help from a well-integrated community than urban-to-urban migrants. Tailored social strategies are needed to target rural-to-urban migrants for addressing mental health disparities among migrant population.

Additionally, our study identified the mediating role of social adaptation on the association between social cohesion and depressive symptoms for both groups. Reflecting the interactions between local residents and migrants, community-level social cohesion impacts whether migrants could "doing well" in the activities of daily living (59) and achieve good psychological wellbeing in the host city.

Our study findings demonstrate that social cohesion matters in mental health outcomes among migrants in China. Improving social cohesion could be an effective social strategy to promote the mental health of the migrant population. Social cohesion is undoubtedly influenced by governance, socio-economic and public policies (26). Thus, public programs and intervention strategies are needed to construct a more integrated community that serves both local residents and internal migrants.

Some limitations of this study need to be acknowledged. First, this study used cross-sectional survey data; we are only able to examine the associations of the variables of interest. First, this study used cross-sectional survey data; we are only able to examine the associations of the variables of interest. From a life-course perspective, the impact of migration and migration-related changes accumulate throughout the life-course; therefore, longitudinal studies are needed for future research. Second, this study was conducted in 10 cities, which is not representative of all migrant-receiving cities in China. Third, to better identify the pathways of social cohesion on depressive symptoms, we need to explore more mediating factors, such as social stress and social exclusion, in future studies. We thus call for future studies to develop and evaluate socio-behavioral interventions in addressing the mental health problems of the increasing number of internal migrants in China.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors. Requests to access these datasets should be directed to millie_qu@163.com.

Ethics statement

The 2017 Urbanization and New Migrant Survey involving human participants were reviewed and

approved by Ethics Committee of Shanghai University (ECSHU 2020-097). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

BW contributed to conceptualization, design, and manuscript preparation. XQu contributed to data analysis and manuscript preparation. XQi, JY, and HZ contributed to manuscript preparation. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Essential oils for treating anxiety: a systematic review of randomized controlled trials and network meta-analysis

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Background and purpose: The findings of clinical studies exploring essential oils (EOs) for anxiety remain disputed, and no studies have yet clarified the differences in the efficacy of EOs. The purpose of the study was to directly or indirectly compare the efficacy of different types of EOs on anxiety by pooling the results of randomized controlled trials (RCTs).

Methods: PubMed, Cochrane Library, Embase, Scopus, Web of Science and the Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched from inception to November 2022. Only full texts of RCTs that investigated the effects of EOs on anxiety were included. The trial data were extracted and the risk of bias was assessed by two reviewers independently. Pairwise meta-analysis and network meta-analysis were performed by Stata 15.1 or R 4.1.2 software.

Results: Forty-four RCTs (fifty study arms) involving 10 kinds of EOs and 3419 anxiety patients (1815 patients in EOs group and 1604 patients in control group) were included. Pairwise meta-analyses showed that EOs were effective in reducing State Anxiety Inventory scores (SAIS) [WMD = −6.63, 95% CI−8.17, −5.08] and Trait Anxiety Inventory scores (TAIS) [WMD = −4.97, 95% CI−6.73, −3.20]. Additionally, EOs could decrease systolic blood pressure (SBP) [WMD = −6.83, (95% CI −10.53, −3.12), $P < 0.001$] and heart rate (HR) [WMD = −3.43, (95% CI −5.51, −1.36), $P < 0.001$]. Network meta-analyses demonstrated that regarding the outcome of SAIS, *Jasminum sambac (L.)Ait. (jasmine)* was the most effective with a weighted mean difference (WMD) of−13.61 (95% CrI−24.79, −2.48). Followed by *Citrus (citrus aurantium L.)*, which had a WMD of−9.62 (95% CrI−13.32, −5.93). Moderate effect sizes were observed for *Rosa rugosa Thunb.* (*damask rose)* (WMD = −6.78, 95% CrI−10.14, −3.49) and *Lavandula angustifolia Mill.* (*lavender)* (WMD = −5.41, 95% CrI−7.86, −2.98). Regarding the results of TAIS, *citrus aurantium L.* was the best ranked intervention with a WMD of−9.62 (95% CrI−15.62, −3.7). Moderate-to-large effect sizes were observed for *Citrus limon (L.) Burm. F.* (*lemon)* (WMD:−8.48; 95% CrI−16.67, −0.33) and *lavender* (WMD:−5.5; 95% CrI−8.7, −2.46).

Conclusion: According to the comprehensive analysis, EOs are effective in reducing both state anxiety and trait anxiety, and *citrus aurantium L.* essential oil seems to be the most recommended type of EO for treating anxiety because of its significant effects in reducing SAIS and TAIS.

Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/, identifier: CRD42022331319.

KEYWORDS

anxiety, aromatherapy, essential oils, State-Trait Anxiety Inventory, network meta-analysis

1. Introduction

Anxiety disorders are one of the most disabling mental disorders and a major contributor to the global burden of disease (1). The prevalence of anxiety disorders is susceptible to political, social, economic and environmental changes, especially in the context of the era of the COVID-19 epidemic in the last 3 years, which has increased the prevalence of anxiety disorders by more than 25% (2, 3).

Currently, benzodiazepines (BDZs) and selective serotonin reuptake inhibitors (SSRIs) remain the cornerstones of treating anxiety disorders. These drugs provide a large short-term benefit, but their long-term efficacy is still limited and may cause certain side effects (4). In this context, complementary and alternative medicine (CAM) therapies are becoming increasingly accepted for their naturalness, affordability and fewer adverse effects. Aromatherapy, as its most important component, uses essential oils (EOs) to effectively balance the mind, body and spirit of the individual (5, 6). EOs are natural products from plants with small molecular weight and certain volatility (7). Essential oil (EO) molecules can affect the hypothalamus, autonomic nervous system and endocrine system (8), improve peripheral blood circulation, regulate blood pressure, pulse and respiration, and ultimately reduce anxiety (9–11).

Recently, a growing number of clinical trials have begun to explore the effects of EOs on anxiety due to various causes. However, the findings of EOs reduce anxiety remained somewhat controversial. Some studies have shown that EOs are effective in relieving anxiety, but others have concluded the opposite. Since the chemical constituents of EOs may vary greatly due to the species, origin place, extraction method, and concentrations in different clinical trials. Furthermore, different intervention procedures can also lead to differences in the effective constituents of which EOs exert their efficacy in the body (12). Therefore, the efficacy of EO may vary in different clinical trials even with the same type of EO. Herein, the efficacy of EOs in alleviating anxiety states still needs to be evaluated by meta-analysis. Of all the types of EOs, lavender is the most extensively studied. There is a meta-analysis has shown that *Lavandula angustifolia Mill.* (*lavender)* EO could ameliorate anxiety and its associated physiological parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and respiratory rate (RR) (13). Interestingly, another meta-analysis concluded that inhalation of *lavender* EO does not significantly reduce SBP (14). Furthermore, conventional pairwise meta-analyses are unable to integrate all the evidence from different types of EOs for anxiety at the same time, making it difficult to comprehensively and systematically evaluate the differences in the efficacy of various EOs and to select the best EO treatment regimen.

Given the limitations of the above studies, we used network meta-analysis combining both direct and indirect evidence to rank essential oils according to State Anxiety Inventory scores (SAIS) and Trait Anxiety Inventory scores (TAIS), and provide evidence-based medical evidence for the adoption of EOs for the treatment of anxiety disorders.

2. Methods

This study was conducted in accordance with the System Preferred Reporting Item Review and Meta-Analysis (PRISMA 2020) guidelines (15). The study was designed to explore the efficacies of common EOs on different causes of anxiety.

2.1. Protocol and registration

The protocol of the review was registered on the International Prospective Register of Systematic Reviews (PROSPERO) with registration number: CRD42022331319.

2.2. Data sources and search strategy

Two investigators (LT and F-FL) independently performed the database search. PubMed, Cochrane Library, Embase, Scopus, Web of Science and the Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched with the terms combined medical subject headings (MeSH) and entry terms: ["oils, volatile"(MeSH) or "essential oils" or "volatile oils" or "aromatherapy" or "odorant"] AND ["anxiety" (MeSH) or "anxious" or "nervousness" or "hypervigilance" or "affect" or "mood" or "PHQ" or "GAD"] AND ("randomized controlled trial" or "clinical trial" or "RCT") from inception to Nov 25, 2022. The detailed search strategies are listed in Supplementary Table S1. Moreover, the reference lists of the included studies and relevant review articles were manually checked to identify potential records that met the established criteria. Searches were not restricted by language.

2.3. Inclusion and exclusion criteria

The inclusion criteria were based on the Participant, Intervention, Comparison, Outcome, and Study design framework: (1) participant: adults (aged $\geq$ 18) with anxiety meet the diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V), or the International Statistical Classification

of Diseases and Related Health Problems 10th Revision (ICD-10), or with scores of at least 20 in the Spielberger State-Trait Anxiety Inventory (STAI) questionnaire (mild anxiety), or have a specific trigger for anxiety and no olfactory problems and no allergies to aromatic substances; (2) intervention: inhalation of EOs (of any duration and frequency) in the trial group; (3) comparison: inhalation of unscented oil or only routine therapy in the control group; (4) outcomes: baseline and post-treatment SAIS, with or without TAIS and vital sign parameters, such as SBP, DBP, HR and RR; and (5) study design: randomized controlled trials (RCTs).

The following exclusion criteria were implemented: (1) the intervention was a mixture of EOs rather than a single type of EO; (2) studies with skewed baseline data for SAIS; (3) articles for which the full text was not available, and studies with incomplete primary outcome data; (4) duplicate publications; (5) studies were published as comments, conference abstracts, or letters to the editor.

2.4. Data extraction and quality assessment

After excluding trials that did not meet the eligibility criteria, two reviewers (LT and F-FL) independently read the full text of the remaining articles, and conducted data collection according to a validated extraction sheet based on the guidance of the Cochrane Handbook for Systematic Reviews of Interventions. The extracted data included: (1) general information (first author, publication year, and country); (2) participants (sample size, mean age, percentage of male participants, and causes of anxiety); (3) content of EOs (type of EO, cumulative duration of intervention, intervention doses); (4) details of the control group; and (5) outcomes (primary: SAIS and TAIS; secondary: SBP, DBP, HR, and RR). Disagreements were resolved through discussing with a third investigator (HQ).

Two reviewers independently assessed the risk of bias of the included studies with the Cochrane Risk of Bias assessment tool (RoB 2.0) (16). The overall risk of bias was classified as high risk (–), unclear risk (?), or low risk (+), based on the following domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, bias in selection of the reported result and overall risk of bias. An adapted version of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool was used to evaluate the quality or confidence of evidence for each outcome by means of a web-based application Confidence in Network Meta-Analysis (CINeMA) (17).

2.5. Data synthesis and statistical analysis

A pair-wise meta-analysis was performed firstly by Der Simonian and Laird method. Then, a quantitative network meta-analysis of with random effects and uninformative priors based on Bayesian theorem was conducted to establish a comprehensive evaluation of the efficacy of EOs in treating anxiety.

The consistency model and the inconsistency model were applied to evaluate the hypothesis of overall consistency between networks in the meta-analysis. Then the deviance information criteria (DIC) of the two models were compared, and the model with the lower DIC value was selected. Subsequently, an ensemble node-split models were used to explore whether there was any statistical local inconsistency between direct and indirect comparisons (P-values $>$ 0.1 indicated local consistency). A consistent model was accepted when there were no inconsistencies. Due to there were closed-loop structures between interventions, we conducted a loop inconsistency test to determine the existence of inconsistency according to the inconsistency factor (IF) value. If the IF value 95% CI contains 0, it indicates that there is no loop inconsistency.

Weighted mean difference (WMD) and 95% confidence interval (CI) were chosen as the effect sizes to report the results of the meta-analysis, while WMD and 95% credibility interval (CrI) as the effect sizes to report the results of the network meta-analysis. A WMD of 0.20 is considered a small difference between the trial and the control group; 0.50, a moderate difference; and 0.80, a large difference. The Higgins I-squared (I^2) index was used to estimate the potential heterogeneity. Random effects models were chosen to compare treatment efficacy considering the clinical and methodological heterogeneity between studies. Each model was calculated by generating 10, 000 sample iterations, with an initial burn-in period of 2, 000 iterations (thin = 1). To rank the interventions, the probability of each intervention being ranked first, second, etc was calculated. The efficacy of each intervention was also ranked by calculating the surface under the cumulative ranking curve (SUCRA).

In view of the significant heterogeneity, exploratory subgroup analyses were conducted based on type of EO, country, cause of anxiety, and accumulative duration of intervention for SAIS, TAIS, SBP, DBP, HR, and RR. Meta-regression analyses were performed based on the accumulative duration of intervention, baseline SAIS and baseline TAIS. Additionally, sensitivity analyses were performed to assess the robustness of the results based on excluding the studies with <30 patients per intervention arm to ensure that large or overestimated treatment benefits were excluded, since small studies tend to have larger effects compared with larger studies. Potential publication bias was evaluated by visual assessment of funnel plots.

Conventional pairwise meta-analyses were performed by STATA version 15.1 (Stata Corp, College Station, TX, USA). Network meta-analyses were conducted using R version 4.1.2 software ("netmeta" and "gemtc" 1.0.1 packages). Network pictures were created to visualize network geometry and node connectivity.

3. Results

3.1. Study selection

The screening process of a PRISMA study flow diagram was shown in Figure 1. We retrieved 5, 553 articles through a systematic search, of which 5, 265 were excluded after a preliminary screening of titles and abstracts since they were completely unrelated to the topic of "essential oil for anxiety". Two hundred and eighty-eight articles were potentially eligible records whose full text was reviewed. Finally, 44 articles were included in present review (14, 18–60).

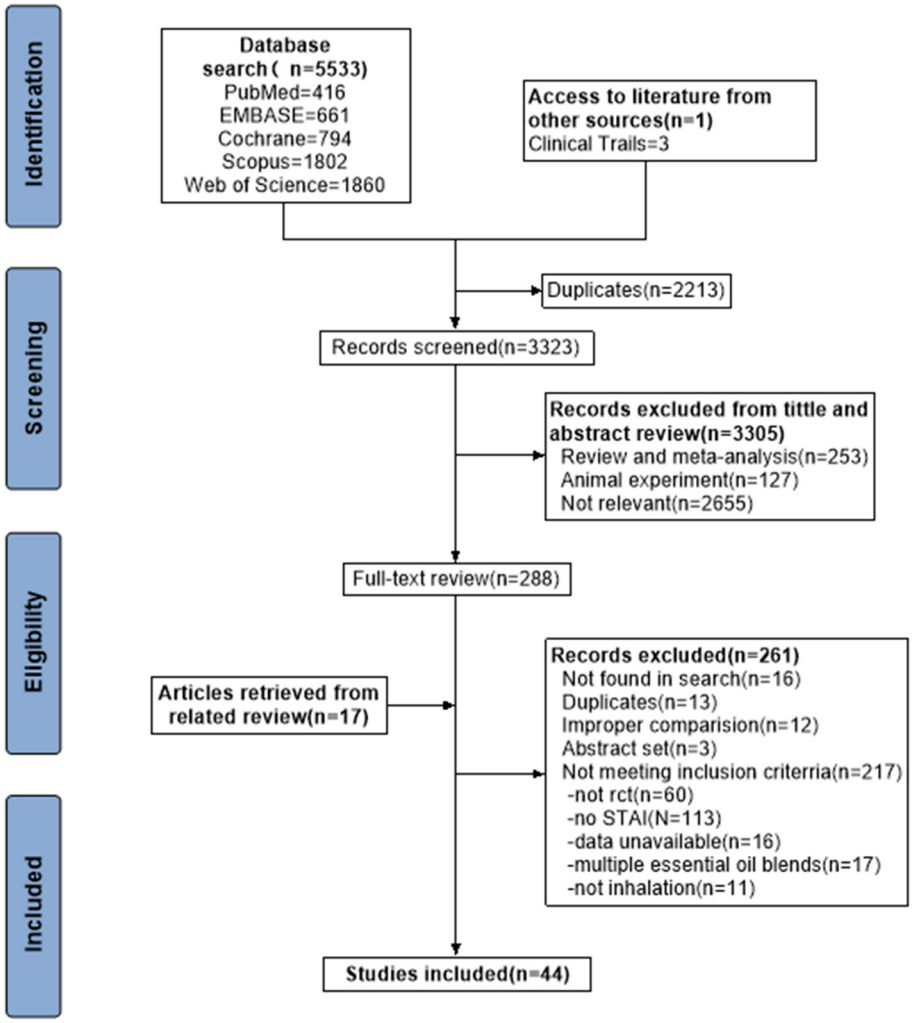

FIGURE 1
Flow diagram of study identification, screening, eligibility assessment, and inclusion.

3.2. Characteristics of included trials

Publication dates ranged from 2010 to 2022 (median, 2016), with 86% of trials published after 2016. Most trials were conducted by Iranian scholars (33/44, 75% trials). The second highest number of trials was conducted in Turkey, with eight. The EOs involved *lavender*, *Rosa rugosa Thunb.* (*damask rose*), *Citrus (citrus aurantium L.)*, *Phyla nodiflora (Linn.) E. L. Greene (lippia alba)*, *Mentha haplocalyx Briq. (mint)*, *Citrus limon (L.) Burm. F.* (*lemon*), *Eucalyptus citriodora Hook. f. (lippia citriodora)*, *Pelargonium hortorum Bailey (geranium)*, *Jasminum sambac (L.)Ait. (jasmine)*, and *Balsam capivi, jesuits'resin (copaiba)*. Fourteen trials explored the effects of EOs on operation-related anxiety, while 12 trials about the invasive examinations induced anxiety. Overall, 44 studies involving 3,419 anxiety patients (1,815 patients in EOs group and 1604 patients in control group) were included (14, 18–60). The detailed characteristics of the studies included in this review were listed in Table 1.

3.3. Assessment of risk of bias

As shown in Figures 2, 3, all included trials were assessed for risk of bias (RoB 2.0) tool. Seventeen studies had a high risk of bias (18, 20, 22, 23, 30, 33, 35, 37, 38, 42–44, 46, 54, 55, 58, 59), and one-quarter of the studies (25%) were at "unclear risk of bias" (24, 25, 27, 29, 31, 32, 36, 45, 48, 50, 51), mostly due to deviations from the intended interventions and selection of the reported results. The remaining 16 studies were at low risk of bias (14, 19, 21, 26, 28, 34, 39–41, 47, 49, 52, 53, 56, 57, 60), with all assessed domains in these studies being at low risk.

3.4. Direct pairwise meta-analysis

3.4.1. State anxiety inventory

Forty-four trials (50 study arms), including 3,419 anxiety patients (1,815 patients in EOs group vs. 1,604 patients in control group), evaluated the effects of EOs on their anxiety by State

TABLE 1 Characteristics of included studies.

Author, year	Country	Participants (EG, CG)		Causes of anxiety	Content of intervention (EG, CG)			Scale	Physiological parameters
		Sample size (male/female)	Mean age (M ± SD or range)		Essential oil type	Duration of intervention	Volume of essential oil		
Abbasijahromi et al. (14)	Iran	EG1:30 EG2:30 CG:30	EG1:29.73 ± 5.29 EG2:26.79 ± 5.53 CG:27.6 ± 5.31	C-section	EG1: Lavender EG2: Damask rose	30 min	3 drops	STAI	NR
Alvarado-García et al. (18)	Perú	EG1:27 (12/15) EG2:27 (12/15) CG:26 (12/14)	EG1:39.50 ± 5.97 EG2:39.84 ± 5.90 CG:39.87 ± 5.85	Spontaneous anxiety	EG1: Lippia alba EG2: Lippia citriodora	30 min	2 drops	STAI	NR
Amzajerdi et al. (19)	Iran	EG:33 (0/33) CG:33 (0/33)	EG:26.97 ± 4.57 CG:28.4 ± 3.91	Pregnant	Mint	280 min	4 drops	SAI	NR
Babatabar Darzi et al. (20)	Iran	EG1:40(25/15) EG2:40(28/12) CG:40 (19/21)	EG1:60.50 ± 5.26 EG2:58.05 ± 5.26 CG:62.27 ± 6.49	Open Heart Surgery	EG1: Damask rose EG2: Lavender	15 min	3 drops	SAI	NA
Bahadori et al. (21)	Iran	EG:30 (12/18) CG:30 (10/20)	EG:31.23 ± 4.41 CG:33.2 ± 7.49	Operating room nurses	Damask Rose	10 min	2 drops	SAI	NR
Bakhsha et al. (22)	Iran	EG:50 CG:50	NR	Preoperative Anxiety	Lavender	1 min	NR	SAI	NR
Beyliklioglu and Arslan (23)	Turkey	EG:40 CG:40	EG:51.48 ± 17.31 CG:48.00 ± 10.63	Before Breast Surgery	Lavender	20 min	3.5 drops	SAI	NR
Eslami et al. (24)	Iran	EG:30 (15/15) CG:30 (15/15)	EG:51.93 ± 7.26 CG:51.47 ± 5.87	Candidates for surgery	*Citrus aurantium* L.	20 min	2 drops	STAI	NR
Eslami et al. (25)	Iran	EG1:30 (15/15) EG2:30 (15/15) CG:30 (15/15)	EG1:51.87 ± 7.81 EG2:51.93 ± 7.26 CG:51.47 ± 5.87	Laparoscopic cholecystectomy	EG1: Lavender EG2: *Citrus aurantium* L.	20 min	2 drops	STAI	NR
Farzaneh et al. (26)	Iran	EG:19 CG:19	EG:49.21 ± 10.63 CG:47.74 ± 15.47	Preoperative Anxiety	Damas Rose	10 min	3 drops	STAI	NR
Fayazi et al. (27)	Iran	EG:36 CG:36	NR	Preoperative Anxiety	Lavender	20 min	2 drops	SAI	NA
Ganji et al. (28)	Iran	EG:44 (32/12) CG:44 (27/17)	EG:46.0 ± 11.5 CG:44.0 ± 13.5	Kidney stones	Damask Rose	15 min	3 drops	SAI	NR
Haddadi et al. (29)	Iran	EG:40 (15/25) CG:40 (17/23)	NR	Myaocardial infarction	Damask Rose	225 min	3 drops	SAI	NR
Hamdamian et al. (30)	Iran	EG:55 CG:55	EG:25.87 ± 5.17 CG:26.24 ± 5.15	During first stage of labor	Damask Rose	30 min	2 drops	SAI	NR

(Continued)

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TABLE 1 (Continued)

Author, year	Country	Participants (EG, CG)		Causes of anxiety	Content of intervention (EG, CG)			Scale	Physiological parameters
		Sample size (male/female)	Mean age (M ± SD or range)		Essential oil type	Duration of intervention	Volume of essential oil		
Hekmatpou et al. (31)	Iran	EG:30 CG:30	NR	Fractured limbs admitted	*Citrus aurantium* L.	360 min	4 drops	SAI	NR
Hu et al. (32)	China	EG:14 (9/5) CG:13 (6/7)	NR	Colonoscopy-related surgery	*Citrus aurantium* L.	5 min	1 drop	SAI	SBP, DBP, RR, HR
Jirdehi et al. (33)	Iran	EG1:35 (15/20) EG2:35 (11/24) CG:35 (19/16)	NR	Candidate for endoscopy	EG1: Lavender EG2: Damask Rose	30 min	2 drops	SAI	NR
Jodaki et al. (34)	Iran	EG:30 (16/14) CG:30 (15/15)	EG:62.8 ± 11.8 CG:61.5 ± 12.75	Cardiac disease	Damask Rose	1440 min	5 drops	SAI	NR
Jokar. et al. (35)	Iran	EG:31 (0/31) CG:31 (0/31)	EG:55.95 ± 5.70 CG:53.56 ± 2.67	Perimenopause	Lavender	560 min	2 drops	STAI	NR
Kasar et al. (36)	Turkey	EG:22 (6/16) CG:22 (3/19)	EG:48.6 ± 12.0 CG:48.1 ± 11.9	Trigger Point Injection	Lavender	12.5 min	5 drops	SAI	NR
Mokhtari et al. (37)	Iran	EG:30 (16/14) CG:30 (15/15)	NR	Burn	Damask Rose	480 min	5 drops	SAI	NR
Moradi et al. (38)	Iran	EG:40 (21/19) CG:40 (24/16)	EG:55.71 ± 1.65 CG:55.95 ± 1.76	Coronary arteriography	*Citrus aurantium* L.	17.5 min	4 mL	SAI	SBP, DBP, RR, HR
Moslemi et al. (39)	Iran	EG:70 (29/41) CG:70 (37/33)	EG:56.76 ± 11.39 CG:56.69 ± 11.37	Acute coronary syndrome	*Citrus aurantium* L.	20 min	1.5 drops	SAI	NR
Ozkaraman et al. (40)	Turkey	EG:30 (6/24) CG:20 (3/17)	EG:57.73 ± 12.81 CG:57.55 ± 12.87	Chemotherapy	Lavender	150 min	3 drops	STAI	NR
Pasyar et al. (41)	Iran	EG:30 (9/21) CG:30 (10/20)	EG:38.10 ± 12.37 CG:38.4 ± 9.58	Laparoscopic cholecystectomy	*Citrus aurantium* L.	20 min	2 drops	SAI	NR
Pimenta et al. (42)	Brazil	EG:14 CG:14	NR	Chronic Myeloid Leukemia	*Citrus aurantium* L.	30 min	10 mL	SAI	SBP, DBP, RR, HR
Rambod et al. (43)	Iran	EG:50 (27/23) CG:50 (28/22)	EG:61.42 ± 14.98 CG:61.84 ± 11.3	Acute myocardial infarction	Lemon	2160 min	5 drops	STAI	SBP, DBP, HR
Reyes et al. (44)	Philippines	EG:25 (14/11) CG:25 (13/12)	EG:52.04 ± 10.38 CG:57.52 ± 13.51	Puncture for hemodialysis patients	*Citrus aurantium* L.	5 min	3 drops	SAI	NR
Sahin et al. (45)	Turkey	EG:36 (19/17) CG:38 (23/15)	EG:50.75 ± 18.02 CG:53.62 ± 11.03	Puncture for hemodialysis patients	Lavender	15 min	5 drops	STAI	NR

(Continued)

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TABLE 1 (Continued)

Author, year	Country	Participants (EG, CG)		Causes of anxiety	Content of intervention (EG, CG)			Scale	Physiological parameters
		Sample size (male/female)	Mean age (M ± SD or range)		Essential oil type	Duration of intervention	Volume of essential oil		
Saritas et al. (46)	Turkey	EG:45 (30/15) CG:45 (26/19)	EG:49.26 ± 14.57 CG:50.62 ± 14.58	ERCP	Lavender	30 min	4 drops	SAI	SBP, DBP, HR
Shirzad et al. (47)	Iran	EG:34 (12/22) CG:34 (14/20)	EG:28.2 ± 7 CG:27.1 ± 5.9	Septorhinoplasy and Rhinoplasty	Lavender	20 min	3 drops	STAI	NA
Soleimani et al. (48)	Iran	EG:32 (16/16) CG:32 (16/16)	NR	acute coronary syndrome	Mint	60 min	3 drops	SAI	NA
Soto-Vásquez et al. (49)	Peru	EG:28 (12/16) CG:27 (13/14)	NR	Spontaneous anxiety	Lippia alba	360 min	4 drops	STAI	NR
Stanley et al. (50)	Singapore	EG:39 (17/22) CG:36 (16/20)	EG:61.6 ± 7.0 CG:63.25 ± 7.7	Cataract Surgery	Lavender	20 min	20 drops	SAI	SBP, DBP, RR, HR, SpO2
Tahmasbi et al. (51)	Iran	EG:45 (18/27) CG:46 (23/23)	NR	Coronary angiography	Lavender	3 min	2 drops	STAI	NA
Tahmasebi et al. (52)	Iran	EG1:33 (12/21) EG2:35 (18/17) CG:33 (14/19)	EG1:60.12 ± 6.79 EG2:57.80 ± 6.21 CG:58.64 ± 6.11	Coronary angiography	EG1: Lavender EG2: *Citrus aurantium* L.	20 min	2 drops	SAI	SBP, DBP, RR, HR, SpO2
Wen et al. (53)	China	EG:50 (17/33) CG:50 (14/36)	EG:47.2 ± 14.5 CG:47.1 ± 14.2	MRI examinations	Lavender	20 min	8 drops	SAI	NR
Fakarian and Tabatabaeichehr (54)	Iran	EG:49 (24/25) CG:48 (21/27)	EG:23 ± 7 CG:21 ± 5	The first stage of labor	Geranium	20 min	NR	SAI	SBP, DBP, RR, HR
Babaii et al. (55)	Iran	EG:30 CG:30	EG:53.63 ± 9.99 CG:56.96 ± 7.89	Cardiac Catheterization	Damask Rose	18 min	NR	STAI	NR
Inci and Çetinkaya (56)	Turkey	EG:48 (30/18) CG:48 (28/20)	EG:60.89 ± 8.74 CG:56.54 ± 11.62	Coronary angiography	Lavender	15 min	5 drops	SAI	SBP, DBP, RR, HR
Karan (57)	Turkey	EG:63 (13/50) CG:63 (17/46)	NR	Oral surgery	Lavender	3 min	NR	SAI	SBP, DBP, RR, HR
Yadegari et al. (58)	Iran	EG:42 (33/9) CG:42 (33/9)	EG:35.55 ± 12.75 CG:36.26 ± 13.39	Laparotomy	Jasmine	60 min	2 drops	SAI	NR
Zhang et al. (59)	China	EG:11 CG:11	NR	Mental Workload	Copaiba	20 min	NR	STAI	NA
Tugut et al. (60)	Turkey	EG:78 CG:78	EG:35.0 ± 9.7 CG:33.5 ± 12.4	Gynecological examination	Lavender	12.5 min	NR	SAI	NR

EG, Experimental group (When there are two controlled trials in the same literature, EG1 and EG2 are used to represent the two experimental groups respectively); CG, Control group; NR, Not Reported; NA, No Analyzed (The study reported, but did not present original data that could be analyzed); STAI, Spielberger State-Trait Anxiety Inventory; SAI, State Anxiety Inventory.

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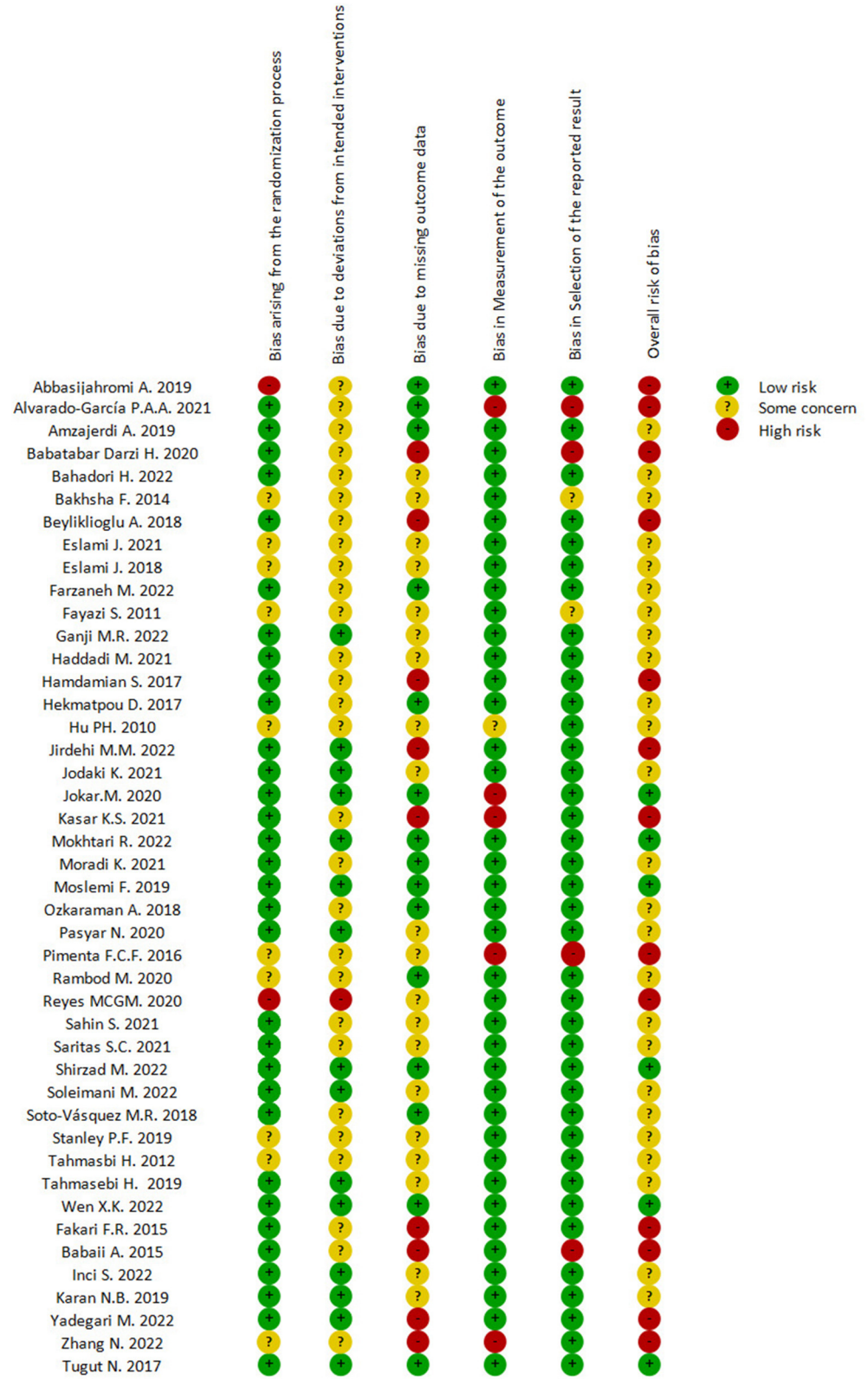

FIGURE 2
Summary of the risk of bias assessment.

Anxiety Inventory (SAI). The pooled WMD showed that EOs therapy led to a significant lower level of state anxiety compared to control group [WMD = −6.63 (95% CI −8.17, −5.08), $P < 0.001$], with moderate heterogeneity ($I^2 = 93.2\%$, $P < 0.001$) (Figure 4).

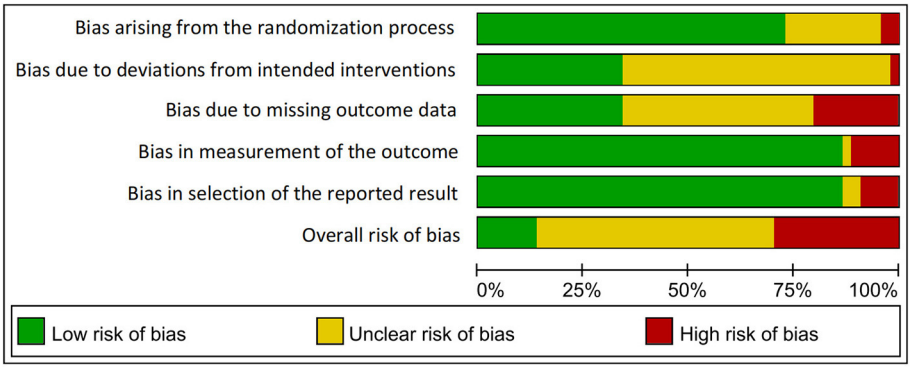

FIGURE 3
Risk of bias graph.

3.4.2. Trait anxiety inventory

A total of 14 studies (17 study arms), including 940 anxiety patients (518 patients in EOs group vs. 422 patients in control group), investigated the effects of EOs therapy on anxiety by Trait Anxiety Inventory (TAI). Pooled effect sizes from the eligible studies indicated that EOs therapy significant lowered the level of trait anxiety compared to control group [WMD = −4.97 (95% CI −6.73, −3.20), $I^2 = 93.9\%$, $P < 0.001$] (Figure 5).

3.4.3. Vital signs

As presented in Figure 6, compared with the control, EOs could decrease SBP [WMD = −6.83 (95% CI−10.53, −3.12), $P < 0.001$] (Figure 6A) and HR [WMD = −3.43 (95% CI−5.51, −1.36), $P < 0.001$] (Figure 6C). The effects of EOs on DBP and RR were also evaluated. EOs had a tendency of decreasing DBP [WMD = −2.11 (95% CI−4.35, 0.13), $P < 0.001$] (Figure 6B) and RR [WMD = −0.53 (95% CI−1.52, 0.46), $P < 0.001$] (Figure 6D), but they were not statistically significant.

3.5. Network meta-analysis

3.5.1. Indirect-comparisons meta-analysis for EOs on state anxiety scores

The network consisted of 38 studies with two arms and 6 studies with three arms reporting on 10 different EOs (20 arms on *lavender*, 11 *damask rose*, 9 *citrus aurantium L.*, two arms each on *lippia alba*, *mint*, and *lemon*, one arm each on *lippia citriodora*, *geranium*, *jasmine*, and *copaiba*, and 50 arms were control groups). The network formed by the direct comparisons between different interventions was shown in Figure 7A.

Comparing the DIC of the consistency and inconsistency models revealed that the consistency model should be used for the analysis ($DIC_{consistency} = 183.12$, $DIC_{inconsistency} = 183.20$).

The effect sizes for the differences between all EOs were presented in league table (Table 2). Figure 8A presented the findings of the indirect-comparisons meta-analysis as effect sizes and their 95% CrI for the different types of EOs interventions on SAIS compared with control group. Four (40%) among 10 interventions significantly decreased SAIS compared with the control group. *Jasmine* was the best ranked intervention with a WMD of−13.61 (95% CrI−24.79, −2.48) for state anxiety. Second only to *jasmine* is *citrus aurantium L.*, which had an effect size of−9.62 (95% CrI−13.32, −5.93). Moderate effect sizes were observed for *damask rose* (WMD = −6.78, 95% CrI−10.14, −3.49) and *lavender* (WMD = −5.41, 95% CrI−7.86, −2.98), compared with the control group. The following interventions had credible intervals including a zero effect, including *mint* (WMD = −6.16, 95% CrI−14.23, 1.83), *lippia alba* (WMD = −6.06, 95% CrI−13.98, 1.81), *lemon* (WMD = −8.22, 95% CrI−19.12, 2.61), *lippia citriodora* (WMD = −4.9, 95% CrI−15.34, 5.48), and *geranium* (WMD = −2.86, 95% CrI−14.19, 8.4).

As shown in Table 3, the SUCRA indicated that *jasmine* was the best ranked intervention with a SUCRA of 88.1. The control intervention had the lowest SUCRA of 11.6 (Figures 9, 10).

There are 3 loops were formed between the pairwise comparisons, and the loop inconsistency test indicated that there was no significant loop inconsistency (Table 4). The node-splitting model test showed no statistical local inconsistency between direct and indirect comparisons ($P > 0.1$). However, the overall heterogeneity remained high (93.2%), indicating that inconsistency did not explain the heterogeneity.

3.5.2. Indirect-comparisons meta-analysis for EOs on trait anxiety scores

This network consisted of 14 RCTs, including 11 studies with two arms and 3 studies with three arms, involving 7 different EOs (7 *lavender*, 3 *damask rose*, two arms each on *citrus aurantium L.* and *lippia alba*, one arm each on *lippia citriodora*, *lemon*, and *copaiba*, and 17 arms were control groups). The most applied EO was *lavender*. The network formed by the direct comparisons between different interventions was shown in Figure 7B.

Comparing the DIC for the consistency and inconsistency models revealed that the consistency model was to be preferred ($DIC_{consistency} = 60.77$, $DIC_{inconsistency} = 60.84$).

The effect sizes for the differences between all EOs on TAIS were presented in league table (Table 2). Figure 8B presented the findings of the indirect-comparisons meta-analysis as effect sizes and their

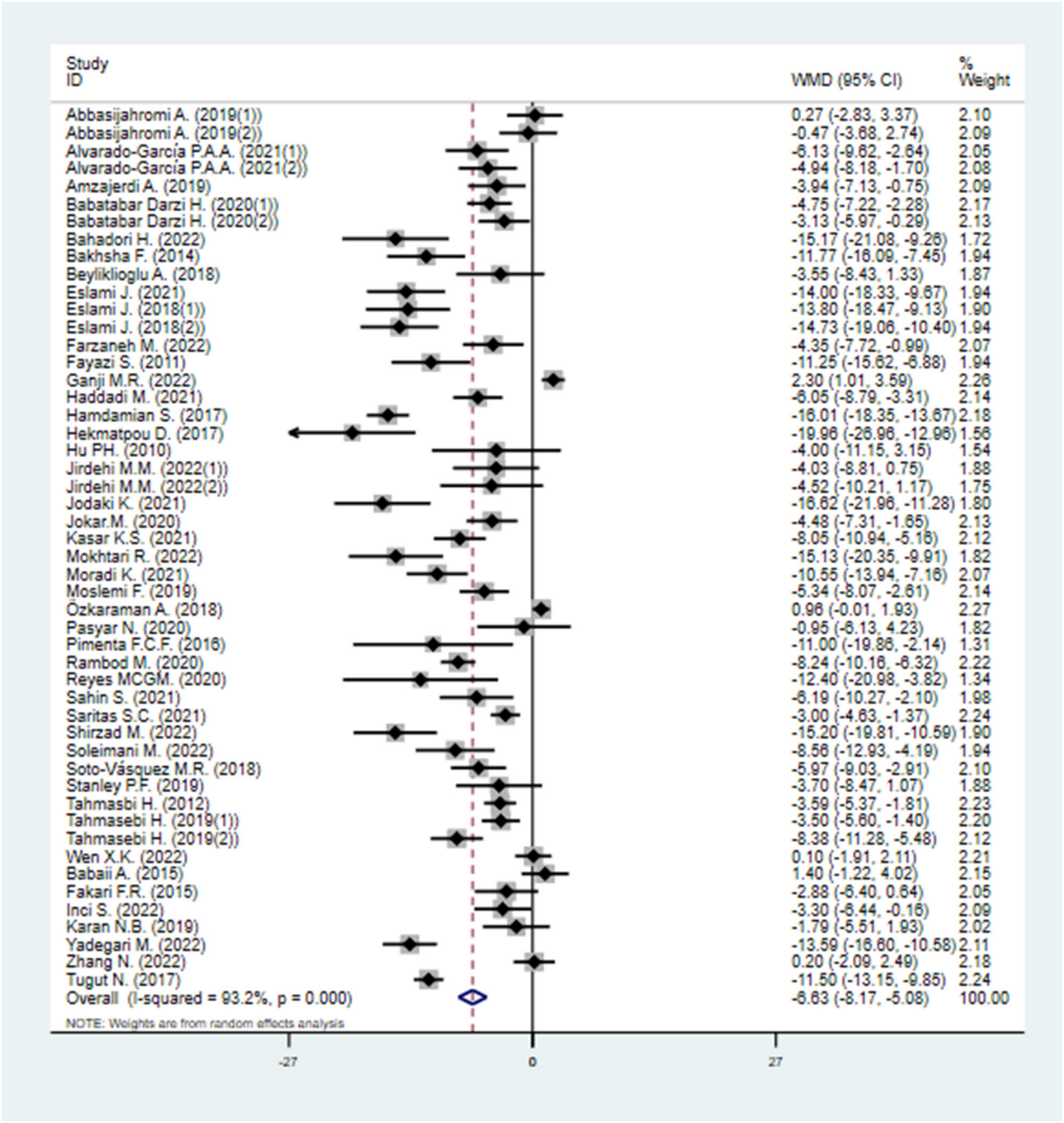

FIGURE 4
Direct pairwise random-effects meta-analyses of SAIS. SAIS, State Anxiety Inventory scores.

95% CrI for the different types of EOs interventions on trait anxiety scores (TAS) compared with control group. Three (43%) among 7 interventions significantly decreased TAS compared with the control group. *Citrus aurantium L.* was the highest ranked intervention with a WMD of −9.62 (95% CrI−15.62, −3.7) for trait anxiety. Moderate-to-large effect sizes were observed for *lemon* (WMD: −8.48; 95% CrI−16.67, −0.33) and *lavender* (WMD: −5.5; 95% CrI−8.7, −2.46). The following 4 interventions had credible intervals including a zero effect, including *lippia alba* (WMD = −4.4, 95% CrI−10.54, 1.77), *lippia citriodora* (WMD = −3.53, 95% CrI−11.64, 4.56), *damask rose* (WMD = −2.64, 95% CrI−7.35, 2.06), and *copaiba* (WMD = 0.2, 95% CrI−8.17, 8.56).

As shown in Table 3, the SUCRA indicated that *citrus aurantium L.* was the highest ranked intervention with a SUCRA of 90.6. The control intervention had the lowest SUCRA of 11.5 (Figures 9, 10).

There are 3 loops were formed between the pairwise comparisons, and the loop inconsistency test indicated that there

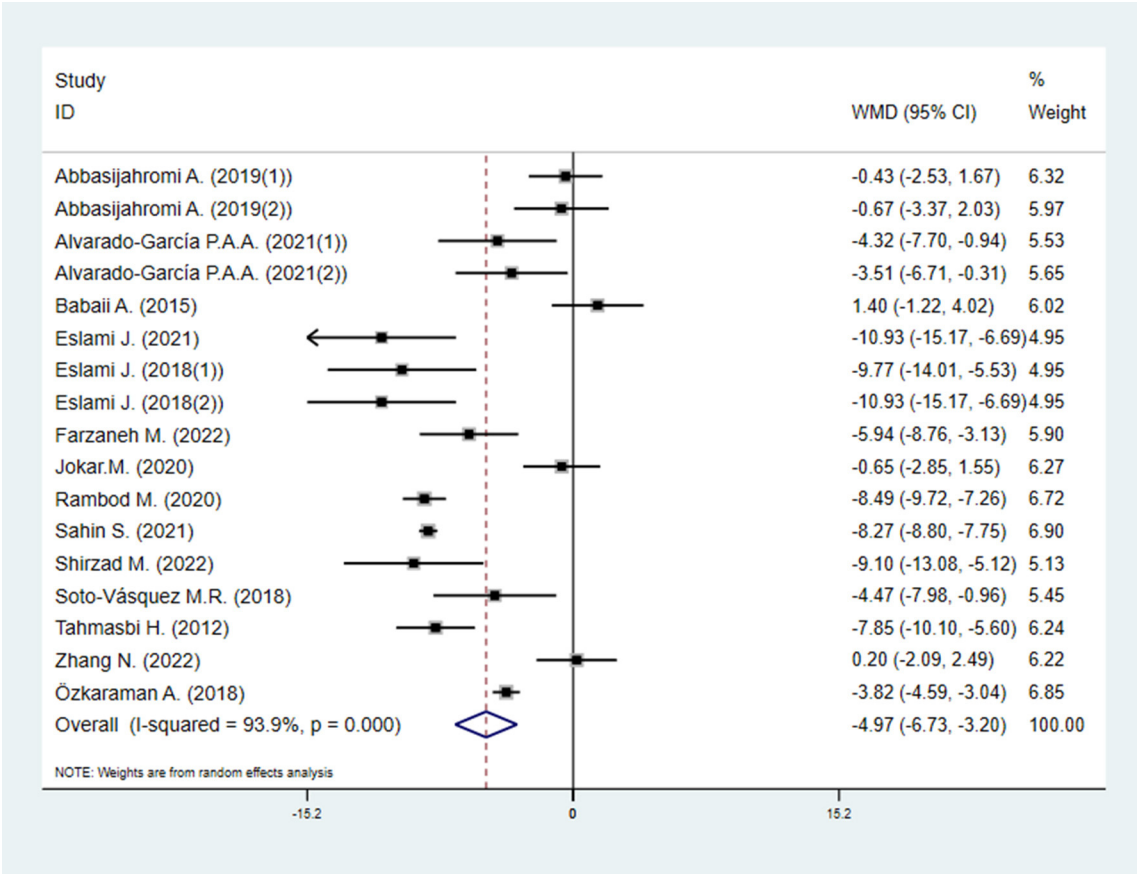

FIGURE 5
Direct pairwise random-effects meta-analyses of TAIS. TAIS, Trait Anxiety Inventory scores.

was no significant loop inconsistency (Table 4). The node-splitting model test confirmed statistical inconsistency between local direct and indirect comparisons ($P < 0.1$), suggesting that inconsistency may explain the overall high heterogeneity ($I^2 = 93.9\%$).

3.6. Subgroup and meta-regression analysis

Subgroup analyses stratified by type of EOs, country, causes of anxiety, and cumulative duration of intervention were performed (Supplementary Table S5 and Figure S5).

According to the results of subgroups by types of EOs, most EOs could significantly reduce SAIS, TAIS, SBP, DBP, HR or RR. However, *citrus aurantium L.* had no significant effect on RR [WMD = −1.402 (95% CI−3.066, 0.263), $P = 0.099$]. *Lemon* could not significantly reduce SAIS [WMD = −8.24 (95% CI−10.16, −6.32), $P = 0.167$] and DBP [WMD = 1.740 (95% CI−2.018, 5.498), $P = 0.364$]. *Mint* failed to reduce SBP [WMD = −0.660 (95% CI−8.673, 7.353), $P = 0.872$], DBP [WMD = 0.530 (95% CI−2.513, 3.573), $P = 0.733$] and HR [WMD = 0.290 (95% CI−0.969, 1.549), $P = 0.652$]. *Lavender* failed to reduce DBP [WMD = −1.627 (95% CI−4.655, 1.401), $P = 0.292$] and RR [WMD = 0.039 (95% CI−0.493, 0.570), $P = 0.887$], and *geranium* had no significant improvement on SAIS [WMD = −2.88 (95% CI−6.40, 0.64), $P = 0.108$], SBP [WMD = 0 (95% CI−7.151, 7.151), $P = 1$], DBP [WMD = −5 (95% CI−10.614, 0.6144), $P = 0.081$] and HR [WMD = 2.000 (95% CI−2.605, 6.605), $P = 0.395$]. *Copaiba* had the weakest efficacy and could not reduce SAIS [WMD = 0.20 (95% CI−2.09, 2.49), $P = 0.864$] and TAIS [WMD = 0.20 (95% CI−2.09, 2.49), $P = 0.395$].

With respect to the country, studies from Iran, Peru, and Turkey found that EOs could significantly reduce SAIS and TAIS. Studies in Brazil and Philippines have only reported that EOs reduced SAIS. However, Turkish studies concluded that EOs had no significant effect on SBP [WMD = −3.527 (95% CI−8.479, 1.425), $P = 0.163$] and HR [WMD = −3.498 (95% CI−9.246, 2.251), $P = 0.233$]. According to the studies of Singapore, EOs could not reduce SAIS [WMD = −3.7 (95% CI−8.465, 1.065), $P = 0.128$], SBP [WMD = −2.880 (95% CI−11.724, 5.964), $P = 0.523$] and HR [WMD = −2.3 (95% CI−7.664, 3.064), $P = 0.401$], and the Chinese study believed that EOs could not reduce SAIS [WMD = −0.033 (95% CI−1.512, 1.445), $P = 0.965$], TAIS [WMD = 0.2 (95% CI−2.090, 2.490), $P = 0.864$], SBP [WMD = −4.050 (95% CI−19.770, 11.670), $P = 0.614$] and HR [WMD = −0.150 (95% CI−9.996, 9.696), $P = 0.976$]. Interestingly, only the Brazilian study concluded that EOs significantly reduced DBP [WMD = −6.4 (95% CI−7.886, −4.914), $P < 0.001$] and RR [WMD = −2.3 (95% CI−2.605, −1.995), $P < 0.001$], while

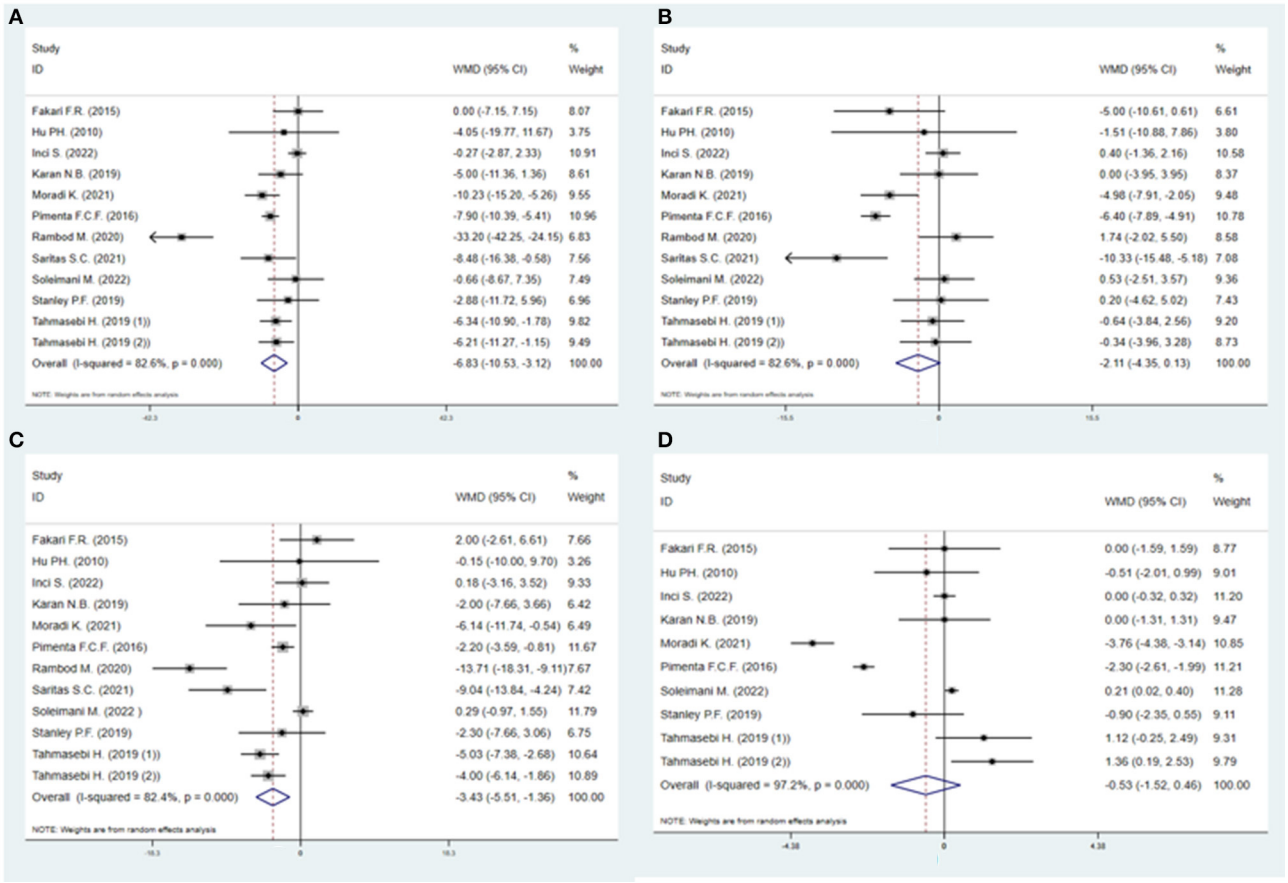

FIGURE 6
Direct pairwise random-effects meta-analyses of vital signs. **(A)** Systolic blood pressure (SBP); **(B)** Diastolic blood pressure (DBP); **(C)** Heart rate (HR); **(D)** Respiratory rate (RR).

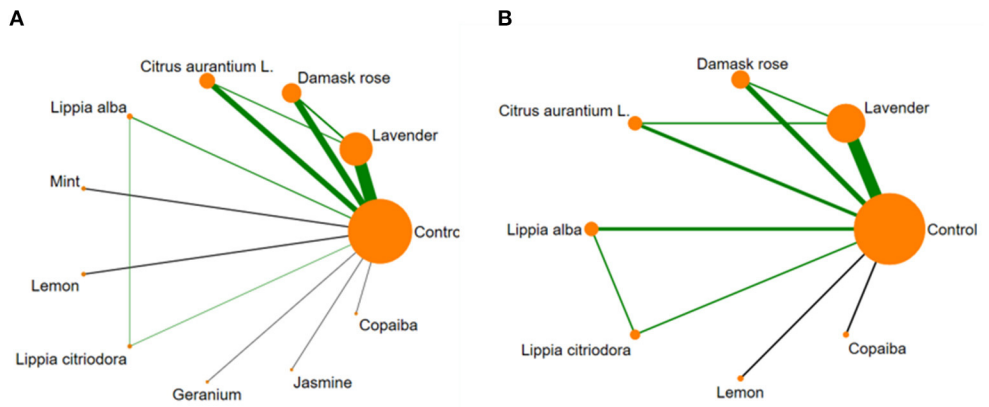

FIGURE 7
Network meta-analysis of available comparisons between 10 essential oils and the control. **(A)** State Anxiety Inventory scores (SAIS); **(B)** Trait Anxiety Inventory scores (TAIS). Line width is proportional to the number of trials that included each pair of treatments (direct comparisons). Circle size is proportional to the total number of participants for each treatment in the network.

other countries found that EOs had no obvious improvement in them.

In causes of anxiety respect, our results showed that EOs could not reduce SAIS in patients with burn-related anxiety [WMD = −15.13 (95% CI−20.354, −9.906), $P = 0.481$] and TAIS in menopause-related anxiety [WMD = −0.650 (95% CI−2.849, 1.549), $P = 0.562$]. EOs were poorly efficacious in delivery-related anxiety, failing to reduce TAIS, SBP, DBP, HR, and

TABLE 2 Network meta-analysis diagram of SAIS and TAIS.

Treatment	Trait anxiety inventory scores										
State anxiety inventory scores	Jasmine	–	–	–	–	–	–	–	–	–	–
	−3.98 (−15.71, 7.71)	*Citrus aurantium* L.	6.98 (−0.48, 14.54)	–	5.24 (−3.36, 13.89)	4.11 (−2.19, 10.41)	5.24 (−3.36, 13.89)	1.13 (−8.93, 11.35)	–	9.82 (−0.38, 20.18)	9.62 (3.7, 15.62)
	−6.82 (−18.45, 4.79)	−2.84 (−7.75, 2.13)	Damask rose	–	−1.76 (−9.5, 6.07)	−2.87 (−8.19, 2.36)	−1.76 (−9.5, 6.07)	−5.84 (−15.26, 3.6)	–	2.84 (−6.72, 12.46)	2.64 (−2.06, 7.35)
	−7.45 (−21.19, 6.22)	−3.46 (−12.28, 5.39)	−0.63 (−9.33, 8.07)	Mint	–	–	–	–	–	–	–
	−7.51 (−21.16, 6.13)	−3.57 (−12.22, 5.14)	−0.71 (−9.28, 7.84)	−0.09 (−11.31, 11.15)	Lippia alba	−1.11 (−8.12, 5.73)	0.85 (−7.32, 9)	−4.08 (−14.37, 6.2)	–	4.61 (−5.84, 15.05)	4.4 (−1.77, 10.54)
	−8.18 (−19.61, 3.18)	−4.22 (−8.43, 0.05)	−1.38 (−5.27, 2.48)	−0.76 (−9.12, 7.64)	−0.64 (−8.94, 7.59)	Lavender	1.11 (−5.73, 8.12)	−2.97 (−11.68, 5.83)	–	5.71 (−3.16, 14.7)	5.5 (2.46, 8.7)
	−8.69 (−24.01, 6.56)	−5.61 (−16.54, 5.23)	−1.88 (−12.82, 9.02)	−1.25 (−14.41, 11.83)	−1.15 (−11.55, 9.2)	−0.51 (−11.18, 10.23)	Lippia citriodora	−4.95 (−16.52, 6.55)	–	3.73 (−7.89, 15.41)	3.53 (−4.56, 11.64)
	−5.37 (−20.88, 10.29)	−1.38 (−12.85, 10.07)	1.45 (−9.94, 12.81)	2.07 (−11.45, 15.62)	2.17 (−11.23, 15.56)	2.83 (−8.34, 13.95)	3.31 (−11.72, 18.46)	Lemon	–	8.69 (−2.99, 20.43)	8.48 (0.33, 16.67)
	−10.76 (−26.63, 5.22)	−6.75 (−18.62, 5.13)	−3.91 (−15.68, 7.85)	−3.31 (−17.14, 10.55)	−3.2 (−17.01, 10.55)	−2.55 (−14.09, 9.05)	−2.06 (−17.39, 13.3)	−5.37 (−21.06, 10.31)	Geranium	–	–
	−13.82 (−29.47, 1.75)	−9.84 (−21.4, 1.7)	−7.01 (−18.42, 4.37)	−6.38 (−19.93, 7.24)	−6.28 (−19.8, 7.24)	−5.63 (−16.84, 5.58)	−5.13 (−20.27, 9.97)	−8.46 (−23.9, 6.97)	−3.08 (−18.85, 12.56)	Copaiba	−0.2 (−8.56, 8.17)
	−13.61 (−24.79, −2.48)	−9.62 (−13.32, −5.93)	−6.78 (−10.14, −3.49)	−6.16 (−14.23, 1.83)	−6.06 (−13.98, 1.81)	−5.41 (−7.86, −2.98)	−4.9 (−15.34, 5.48)	−8.22 (−19.12, 2.61)	−2.86 (−14.19, 8.4)	0.22 (−10.72, 11.16)	Control

SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores. The orange represents the different types of essential oils. The green represents the effect size of essential oils that significantly decrease SAIS or TAIS.

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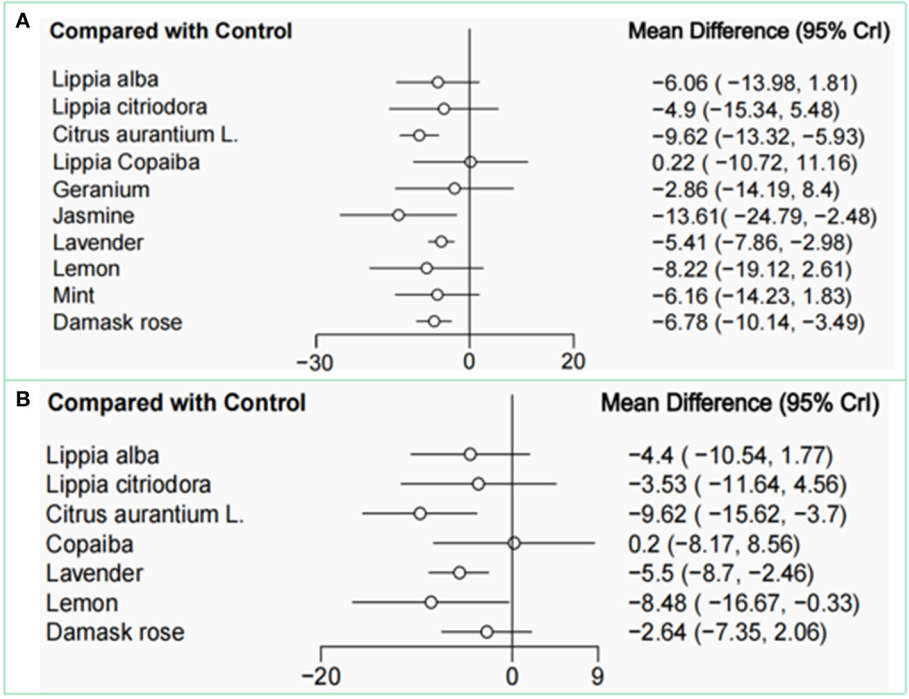

FIGURE 8
Network meta-analysis for comparisons with the control group of SAIS **(A)** and TAIS **(B)**. SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores.

RR. Similarly, EOs had no significant effect on TAIS [WMD = −3.250 (95% CI−12.315, 5.815), $P = 0.482$], DBP [WMD = −2.745 (95% CI−5.952, 0.462), $P = 0.093$], and RR [WMD = −0.362 (95% CI−2.698, 1.974), $P = 0.761$] in patients with invasive examination-related anxiety. EOs could not improve the physiological parameters of operation-related anxiety, including SBP [WMD = −4.256 (95% CI−9.159, 0.648), $P = 0.089$], DBP [WMD = −0.072 (95% CI−2.977, 2.832), $P = 0.961$], HR [WMD = −1.887 (95% CI−5.508, 1.735), $P = 0.307$], and RR [WMD = −0.434 (95% CI−1.249, 0.381), $P = 0.296$]. Additionally, EOs did not have apparent effects on SBP [WMD = −16.859 (95% CI−48.747, 15.029), $P = 0.3$], DBP [WMD = 1.009 (95% CI−1.356, 3.374), $P = 0.403$], and HR [WMD = −6.528 (95% CI−20.243, 7.187), $P = 0.351$] in cardiovascular disease-induced anxiety.

Regarding the cumulative duration of intervention, we found that the general efficacy of EOs for anxiety was optimal when the cumulative duration of intervention was 10∼30 min, which could not only effectively reduce SAIS [WMD = −5.815 (95% CI−7.779, −3.851), $P < 0.001$] and TAIS [WMD = −4.935 (95% CI−7.882, −1.989), $P < 0.001$], but also stabilize vital signs, including lowering SBP [WMD = −5.372 (95% CI−8.484, −2.259), $P = 0.001$], DBP [WMD = −3.235 (95% CI−6.002, −0.467), $P = 0.022$], and HR [WMD = −3.184 (95% CI−5.050, −1.318), $P = 0.001$]. In fact, EOs reduced SAIS regardless of the duration of the intervention, as evidenced by further meta-regression analysis ($P > 0.05$). However, EOs had no significant effect on SBP, DBP, and HR when the cumulative duration of intervention was <10 min or maintained at 30∼100 min, and had no improvement on TAIS when it was >500 min [WMD = −4.625 (95% CI−12.307, 3.057), $P = 0.238$]. Meta-regression analysis confirmed that the effect size of EOs in lowering DBP was significantly negatively correlated with the intervention time when it was within 30 min (regression = −2.70, $P = 0.027$). Additionally, the effect size of EOs in lowering SBP and HR also showed a negative trend with the intervention time when it was controlled within 30 min, but it was not statistically significant ($P > 0.05$) (Table 5).

3.7. Sensitivity analysis

In the sensitivity analyses to test the effect of smaller sample sizes on the overall weighted mean in the "State Anxiety Inventory" studies, the effect sizes of most comparisons were decreased. The overall effect size for EO interventions on SAIS was reduced from −6.63 to −0.84 when excluding smaller studies, although none of the confidence intervals included the zero effect. Additionally, the exclusion of small studies did not generate a reduction in heterogeneity (Supplementary Figure S6A).

Interestingly, in the sensitivity analyses to test the effect of smaller sample sizes on the overall weighted mean, studies using the Trait Anxiety Inventory as an evaluator showed the same effect size trends as the State Anxiety Inventory. The overall effect size for EO interventions on TAIS was reduced from −4.97 to −1.51 when excluding smaller studies, and none of their credible intervals

included the zero effect. The exclusion of small studies did not decrease the heterogeneity (Supplementary Figure S6B).

3.8. Publication bias

Supplementary Figure S7 presented the funnel plot of the publication bias. The distribution of most dots in the figure was relatively symmetrical and uniform, indicating little evidence of publication bias. However, there are some dots distributed outside of the 95% CI, suggesting the effect of small sample size may exist.

3.9. Certainty of evidence

CINeMA application was used to conduct GRADE judgments. The therapeutic effect of EO on anxiety was measured by SAI inventory, twenty-six of comparisons were judged to be low rating, with twenty-nine very low comparisons while measured by TAI inventory, eighteen of comparisons were judged as low rating, with ten very low comparisons (Supplementary Tables S3.1, S3.2).

4. Discussion

4.1. Main study findings

To the best of our knowledge, this was the first study about different EOs for treating anxiety using Bayesian network meta-analysis. Anxiety was assessed with the Spielberger State-Trait Anxiety Inventory (STAI), which is currently the most extensively used inventory for evaluating anxiety levels and consists of two parts, SAI and TAI. The changes of SAIS and TAIS were used as the primary outcomes to evaluate the therapeutic effects of EOs on anxiety in this study. Pairwise meta-analyses indicated that EOs could effectively reduce SAIS and TAIS. Further network meta-analyses showed that *jasmine* was the most effective EO in reducing SAIS, followed by *citrus aurantium L.*, which ranked first in reducing TAIS.

Vital signs are considered to be important physiological indicators of anxiety indirectly (13). Emotional signals of anxiety are sent from the amygdala and hippocampus of the limbic system to the hypothalamus, activating the hypothalamic-pituitary-adrenocortical (HPA) axis (61). Moreover, anxiety could cause increased sympathetic excitability, which leads to increased blood pressure, HR and RR. Herein, vital signs may be helpful in objective assessment of anxiety. Our results found that EOs dramatically reduced SBP and HR, and had a tendency to lower DBP and RR, but were not statistical significance.

4.2. Possible explanation for study findings

Our findings were consistent with previous conventional meta-analyses focusing on EOs for anxiety. Indicating that EOs significantly alleviate anxiety (62, 63). Additionally, our results further confirmed the results of a previous meta-analysis pooling animal experiments from a clinical perspective (64).

TABLE 3 Ranking of values of SUCRA for SAIS and TAIS.

Treatment	SUCRA	PrBest	MeanRank
SAIS			
Control	11.6	0	9.8
Lavender	45.4	0	6.5
Damaskrose	57.9	0.5	5.2
CitrusaurantiumL	79.3	8.7	3.1
Lippiaalba	52	3.1	5.8
Mint	53.2	4.1	5.7
Lemon	64.5	15.6	4.6
Lippiacitriodora	45.3	4.8	6.5
Geranium	33.9	3.2	7.6
Jasmine	88.1	59.1	2.2
Copaiba	19	0.7	9.1
TAIS			
Control	11.5	0	7.2
Lavender	63.8	1.5	3.5
Damaskrose	36.3	0.1	5.5
CitrusaurantiumL	90.6	55.2	1.7
Lippia alba	53.1	2.8	4.3
Lippia citriodora	45.3	3.8	4.8
Lemon	81.9	36.2	2.3
Copaiba	17.4	0.4	6.8

SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores.

Pairwise meta-analyses suggested that EOs had a stronger total therapeutic effect on state anxiety than trait anxiety. This was consistent with the results of an earlier meta-analysis (65). Moreover, we further found that EOs were effective in reducing state anxiety regardless of the cumulative duration of the intervention. However, EOs could not alleviate trait anxiety when the cumulative intervention time exceeded 500 min, with the largest effect size within 10 min of the intervention time. Thus, the efficacy of EOs on trait anxiety was more inclined to immediate intervention. The reason for these results may be related to the mechanisms of state anxiety and trait anxiety. Previous study has shown that state anxiety and trait anxiety are mapped differently in the brain (66). State anxiety is a transient intense emotional state associated with a temporary increase in sympathetic nervous system activity without a specific pathological condition, and it can disappear with the removal of stress or danger (66). Trait anxiety is a personality tendency that remains stable over time (67). It may be associated with different psychopathological conditions and continuous high arousal. It does not disappear easily when the stress is relieved, and people with high trait anxiety are easy to develop anxiety disorders (68). Therefore, EOs have a more obvious therapeutic effect on state anxiety. Trait anxiety symptoms could restore to their stable personality characteristics soon, although a short period of EOs stimulation can effectively alleviate them.

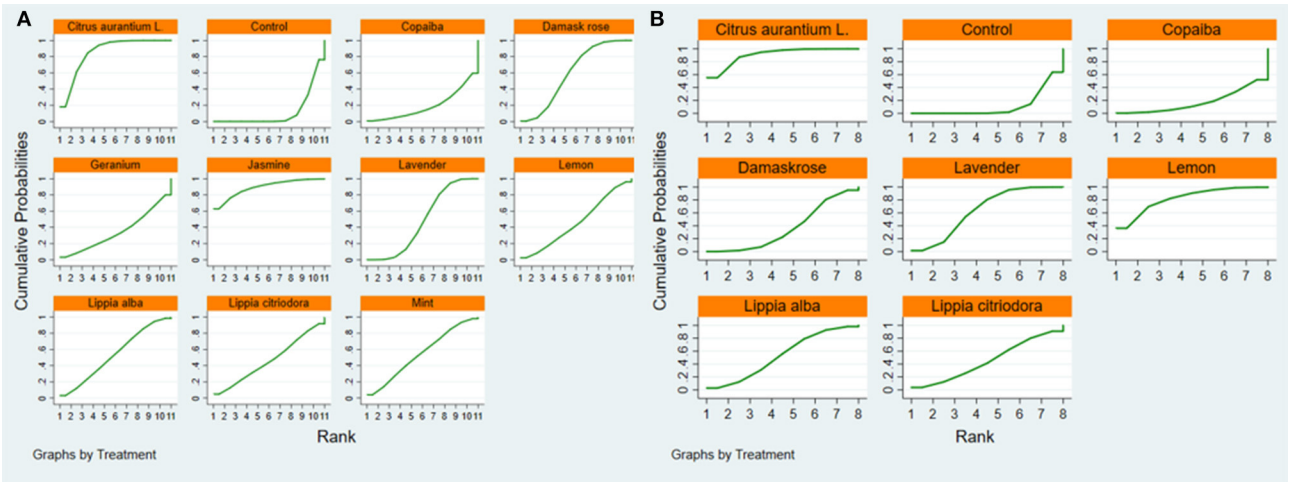

FIGURE 9
SUCRA figure of SAIS **(A)** and TAIS **(B)**. Note: SUCRA = surface under the cumulative ranking. SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores.

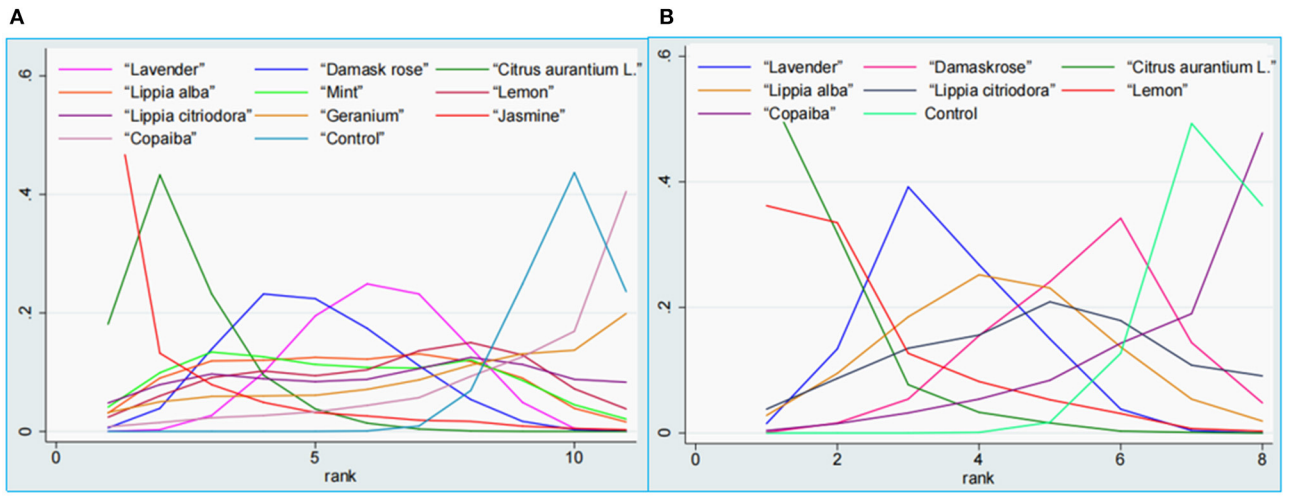

FIGURE 10
Ranking probability plot of SAIS **(A)** and TAIS **(B)**. SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores.

TABLE 4 Loop-specific approach.

Outcomes	Loop	IF	seIF	*z*-value	*p*-value	CI_95	Loop_Heterog_tau^2
SAIS	Con-Lav-Dam	2.14	4.02	0.79	0.43	(0.00, 10.06)	20.88
	Con-Lav-Cit	1.33	4.15	0.32	0.75	(0.00, 9.46)	31.66
	Con-Alb-Citrio	0.16	2.81	0.06	0.96	(0.00, 5.67)	0.00
TAIS	Con-Lav-Dam	4.87	4.43	1.10	0.27	(0.00, 13.55)	10.06
	Con-Lav-Cit	4.85	5.03	0.96	0.34	(0.00, 14.70)	11.32
	Con-Alb-Citrio	0.15	2.97	0.05	0.96	(0.00, 5.96)	0.00

SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores; Con, Control; Lav, Lavender; Dam, Damask rose; Cit, Citrus aurantium L.; Alb, Lippia alba; Citrio, Lippia citriodora.

Network meta-analyses suggested that that *jasmine* was the strongest type of EO for reducing SAIS. Contrary to previous studies that suggested that *jasmine* could only improve nervousness and not reduce symptoms of anxiety and stress (58), our study found that *jasmine* significantly improved state anxiety symptoms and thus reduced SAIS. Pharmacological studies suggested that the

TABLE 5 Meta-regression of weighted mean difference according to cumulative duration of intervention.

Effect size	Coef.	Std. Err.	t	P>|t|	95% CI	tau^2	Adj R-squared (%)
SAIS	−0.003	0.002	−1.42	0.163	−0.007∼0.001	25.34	1.68
TAIS	−0.001	0.002	−0.58	0.571	−0.005∼0.003	15.01	−4.82
SBP	−0.178	0.162	−1.10	0.304	−0.550∼0.195	7.131	13.88
DBP	−0.296	0.110	−2.70	0.027	−0.549∼-0.043	3.789	58.81
HR	−0.137	0.131	−1.05	0.326	−0.439∼0.165	5.275	−15.56

SAIS, State Anxiety Inventory scores; TAIS, Trait Anxiety Inventory scores; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

mechanisms by which *jasmine* reduced SAIS may be related to the increase of β wave in the frontal cortex center and left occipital cortex caused by olfactory stimulation (69). However, only one study explored the efficacy of *jasmine* on anxiety, so the credibility of this result is low and more researches are indispensable to confirm this result.

Considering that there was only one RCT reporting *jasmine* for anxiety, the results may be highly biased and less credible. *Citrus aurantium L.* (85.6%) and *jasmine* (89.3%) had similar efficacy in reducing SAIS according to SUCRA values, and *citrus aurantium L.* ranked first in reducing TAIS. Furthermore, *citrus aurantium L.* could dramatically reduce the objective indicators reflecting anxiety, including SBP, DBP, and HR. The anxiolytic activity of *citrus aurantium L.* was mediated by the serotonergic system (5-HT1A receptor) (7, 70). Interestingly, *citrus aurantium L.* significantly ameliorated anxiety and did not interfere with physiological levels of melatonin and corticosterone (71). Thus, it could be reasonably inferred that *citrus aurantium L.* EO has the greatest benefits in treating anxiety.

Previous studies on the treatment of anxiety with lemon EO are still somewhat controversial. An RCT investigating the effect of lemon EO on anxiety during the active phase in primiparas showed that lemon EO had no effect on anxiety (72). However, another multicenter, assessor-blinded trial demonstrated the efficacy of aromatherapy with lemon EO inhalation in relieving anxiety (43). To the best of our knowledge, this study was the first meta-analysis of lemon EO for anxiety. Our paired meta-analysis confirmed that lemon EO significantly ameliorated trait anxiety, but did not alleviate state anxiety. Further, our network meta-analysis found that *lemon* ranked second among all EOs in the aspect of reducing TAIS. The main component of *lemon* is s-limonene. The anti-trait anxiety effect of *lemon* is closely related to the 5-serotonergic pathway, particularly through the 5-HT (1A) receptor. In addition, *lemon* significantly accelerated the metabolic turnover of dopamine (DA) in the hippocampus and 5-HT in the prefrontal cortex and striatum (69).

Current network meta-analyses also found that *damask rose* was the third most anti-anxiety EO after *jasmine* and *citrus aurantium L.* in reducing SAIS. However, *damask rose* could not reduce TAIS. This finding was in line with a previous meta-analysis that pooled the studies about *damask rose* mill on anxiety, indicating that *damask rose* dramatically decreased state anxiety but had no obvious effect on trait anxiety (73). *Damask rose* mainly contains isoflavones. On one hand, isoflavones can directly bind to GABA receptors to reduce anxiety (74). On the other hand, isoflavones inhibit inducible nitric oxide synthase (iNOS) and then reduce the production of nitric oxide, which regulates the concentration of neurotransmitters such as serotonin, dopamine, norepinephrine and glutamate, and inhibits the activation of soluble guanylate cyclase, which in turn reduces the production of cyclic guanosine monophosphate (cGMP), thereby reducing anxiety (75).

The number of studies using *lavender* as an intervention were the largest for both state anxiety and trait anxiety. Our results indicated that the efficacy of *lavender* in reducing SAIS and TAIS was comparable. This was consecutive with the results of previous meta-analyses (12, 13). Researches in pharmacology have found that the anxiolytic effects of *lavender* are related to the interaction of its monoterpene components such as linalool and linalyl acetate with NMDA receptors. Additionally, the anxiolytic effect could be partially attributed to its inhibition of serotonin transporter (SERT) and protection of SH-SY5Y cells from hydrogen peroxide-induced neurotoxicity (76).

Results of an RCT using *mint* intervention in emergency cardiac patients found that *mint* reduced anxiety and its induced increase in respiratory rate. In keeping with this, our study indicated that *mint* could significantly reduce SAIS. *Mint* affects the hypothalamus by stimulating the olfactory pathway, which reduces the secretion of adrenocorticotropin-releasing hormone, adrenocorticotropin and cortisol, ultimately reducing anxiety (77, 78).

Finally, the results of our study showed that neither *geranium* nor *copaiba* could reduce anxiety, and *copaiba* ranked the worst. However, the RCTs on *geranium* and *copaiba* for anxiety each only one was included, which tends to cause significant heterogeneity, so these results should be interpreted with caution and more studies are needed to confirm these conclusions in the future.

No adverse events were reported in any of the trials, and their safety remains uncertain. EOs gas molecules can be inhaled and then transported to the central nervous system after entering the bloodstream through the lung, or they can cross the neuronal network of the olfactory system and directly reach and act on the corresponding brain areas, causing activation in different brain regions to induce anxiolytic effects (8). Several studies concluded that EOs appeared to be well tolerated, as inhalation of different doses of EOs did not cause changes or show signs of toxicity (48).

In summary, the most effective was *jasmine* intervention with a cumulative duration of 30 to 100 min for state anxiety, while *citrus aurantium L.* intervention with a cumulative duration of 10 min or less were most efficacious for trait anxiety. Nevertheless, combining

self-reported SAIS and TAIS with objective indicators, a cumulative intervention of 10 to 30 min with *citrus aurantium L.* was optimal, because it reduced not only SAIS and TAIS, but also SBP, DBP, and HR. However, it is worth noting that due to the lack of reports on adverse effects, the studies with EOs included in this study could not be fully used to rank the safety of EOs. This limitation requires special attention in future studies.

4.3. Strength and limitations

The current study has several strengths. We developed rigorous eligibility criteria, conducted a comprehensive search, assessed the risk of bias, addressed key outcomes, performed valuable sensitivity and subgroup analyses, and rated the certainty of the evidence using CINeMA by GRADE criteria. For the first time, a network meta-analysis was used to compare the differences in efficacy of various types of commonly used EOs, providing clinicians with a rational choice of essential oils for the treatment of anxiety.

However, the study also had a number of limitations. To comprehensively summarize the efficacy of EOs, we included a wide range of interventions that varied in terms of number of interventions, duration, dose, co-morbidities, or causes of anxiety, so that there may be large heterogeneity across trials. Moreover, most of the trials had a high risk of bias and low or very low quality of evidence. Therefore, the credibility of the results was low and we need to be cautious in interpreting the results. In addition, the intrinsic characteristics of EOs, such as the species, place of origin, and the intervention procedures of EOs, including extraction method, exposure concentration, method of exposure, duration of exposure, and route of administration, could affect the amount of active ingredients of EOs in the body and thus the efficacy of EOs. Thus, only by controlling for these variables can the efficacy of EOs for anxiety in different clinical trials be more accurately determined. What's more, more high-quality RCTs that rigorously document the characteristics and intervention procedures of EO, may be needed in the future to improve the reliability of meta-analysis conclusions.

5. Conclusion

This study confirmed that EOs may be effective in treating anxiety, and *citrus aurantium L.* appeared to be the most recommended type, as it showed a large effect size in reducing both SAIS and TAIS. However, due to the obvious heterogeneity among the included studies, our results should be interpreted with caution and more high-quality RCTs are expected to confirm this result in the future.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

LT and F-fL: conceptualization, visualization, investigation, and writing-original draft. L-zL and C-gF: conceptualization, visualization, and writing – review and editing. X-cM: investigation and writing – review and editing. Y-xP: formal analysis and writing – review and editing. J-mL and HQ: funding acquisition and writing – review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1144404/full#supplementary-material

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Prevalence of depression and its correlation with anxiety, headache and sleep disorders among medical staff in the Hainan Province of China

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Objective: This cross-sectional survey aimed to investigate the prevalence of depression among medical staff and its risk factors as well as the association between depression, anxiety, headache, and sleep disorders.

Methods: Stratified random cluster sampling was used to select medical staff from various departments of four hospitals in Sanya City. The Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), and Pittsburgh Sleep Quality Index (PSQI) were used to quantitatively assess depression, anxiety, and sleep disorders. Correlation and regression analyses were performed to determine factors affecting the depression occurrence and scores.

Results: Among 645 medical staff members, 548 (85%) responded. The 1-year prevalence of depression was 42.7% and the prevalence of depression combined with anxiety, headache, and sleep disorders was 23, 27, and 34.5%, respectively. The prevalence of depression in women, nurses, the unmarried or single group, and the rotating-shift population was significantly higher than that in men (48.3% vs. 27.1%, odds ratio OR=2.512), doctors (55.2% vs. 26.7%, OR=3.388), the married group (50.5% vs. 35.8%, OR=1.900), and the day-shift population (35.2% vs. 7.5%, OR=1.719). The occurrence of depression was correlated with anxiety, sleep disorders, headache, and migraines, with anxiety having the highest correlation (Spearman's Rho=0.531). The SDS was significantly correlated with the SAS and PSQI (Spearman's Rho=0.801, 0.503) and was also related to the presence of headache and migraine (Spearman Rho=0.228, 0.159). Multiple logistic regression indicated that nurse occupation and anxiety were risk factors for depression, while grades of anxiety, sleep disorders and nurse occupation were risk factors for the degree of depression in multiple linear regression.

Conclusion: The prevalence of depression among medical staff was higher than that in the general population, especially among women, nurses, unmarried people, and rotating-shift workers. Depression is associated with anxiety, sleep disorders, headache, and migraines. Anxiety and nursing occupation are risk factors for depression. This study provides a reference for the promotion of occupational health among medical professionals.

KEYWORDS
prevalence, depression, anxiety, headache, sleep disorders (SD), medical staff

1. Introduction

The 2019 global burden of diseases study reported that depression ranked second in years lived with disability and headache disorders ranked third among all age groups and both sexes (1, 2). The global incidence of depression is rapidly increasing. The World Health Organization predicts that depression will become a primary disease burden by 2030.

A survey of adults with mental disorders covering 31 provinces and cities in China from 2013 to 2015 showed that the lifetime prevalence of depressive disorders in Chinese adults was 6.8%; however, only 0.5% of patients received adequate treatment (3). Faced with high-intensity and demanding work, medical staff often suffer from depression, anxiety, headache, and sleep disorders, which not only cause pain to individuals and families but also affect work efficiency, social productivity, and cause social burden. A meta-analysis of clinical studies and population surveys from 2000 to 2020 suggested that the primary headache comorbidities included depression, hypertension, anxiety, diabetes, and sleep disorders (4). Thus, depression, anxiety, headache, and sleep disorders are highly prevalent and often interact with each other but are not fully recognized or treated.

Our research team conducted an epidemiological survey on the prevalence of primary headache among medical staff in Sanya city, Hainan province, and found that the prevalence of primary headache among medical staff was higher than that among the general population (5). Based on a previous investigation, we added depression- and anxiety-related score data and investigated the correlation between depression, anxiety, headache, sleep disorders, and the risk factors for depression to provide data for improving the health status of medical staff.

2. Materials and methods

2.1. Survey methods

This is a cross-sectional study. The research protocol was approved by the Ethics Committee of the Chinese PLA General Hospital. All patients were informed of the purpose of the study and provided informed consent prior to participation.

The survey subjects were medical staff who were randomly selected from three tertiary hospitals (Hainan Hospital of Chinese PLA General Hospital, Third People's Hospital of Hainan Province, and People's Hospital of Sanya) and one secondary hospital (Chinese PLA No. 425 Hospital) in Sanya, South China, from May 2018 to October 2018. After a preliminary survey of one department in each hospital, stratified random cluster sampling was performed using epidemiological methods. The departments in all hospitals were divided into three groups: internal medicine, surgery, and others (Emergency Department and Radiology Department), and eight clinical departments were randomly selected. Physicians and nurses were selected as a whole group for this investigation. The survey was divided into two parts: a questionnaire and an interview (face-to-face and telephone). All participants who reported depression, anxiety, headache, or sleep disorders were interviewed by neurological and psychiatric specialists after reviewing their questionnaires. The notes associated with the questionnaire were explained and the participants' questions were answered in reference to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition and the International Classification of Headache Disorders, Third Edition criteria. Each participant answered the structured questionnaires, and data were collected on demographics, occupation-related factors, and characteristics such as depression, anxiety, headache, and sleep disturbance over the past year.

2.2. The questionnaire

The questionnaire consists of four parts.

A. Demographic data and medical professional characteristics included sex, age, marital status (single or divorced, married), body mass index (BMI, graded as underweight, normal weight, overweight, obese), educational background (college or lower, bachelor's degree, master's degree, or above), occupation (doctor or nurse), work seniority, professional titles (junior, senior, or advanced), work arrangements (day-shift or rotating shift), and number of night shifts. For this part, we referred to the results of our previous survey (5).
B. The Self-Rating Depression Scale (SDS) and the Self-Rating Anxiety Scale (SAS) included 20 items that measured mental, physical, and emotional symptoms and were rated by respondents in terms of how often the symptoms were experienced over the past week, using a 4-point scale ranging from 1 (none or very little) to 4 (most or all of the time). The raw score was calculated and converted into a standard score. The SDS scores were interpreted as follows: 53–62, mild depression symptoms; 63–72, mild, moderate depression symptoms; and > 72, severe depression symptoms. SAS scores of 50–59 were classified as mild anxiety, 60–69 as moderate anxiety, and > 69 as severe anxiety. Both scoring systems have been shown to have good internal consistency, and the Cronbach alpha coefficients of the two scores were 0.81 and 0.82, respectively (6). Wang, Cai, and Xu (7) suggested that an index score of 53 (raw score 42) for depression was more appropriate for Chinese populations and this score has since been widely adopted (8, 9). At this score sensitivity is 96.5% and specificity 59.3% according to the Dunstan and Scott's research (10).
C. The headache profile section (25 questions) included headache nature, headache degree (visual analogue scale, VAS), headache frequency, accompanying symptoms, and aggravating and

Abbreviations: BMI, body mass index; OR, odds ratio; PSQI, pittsburgh sleep quality index; SAS, self-rating anxiety scale; SDS, self-rating depression scale; TTH, tension-type headache; VAS, visual analog score.

alleviating factors. The reliability and validity of the Chinese version of the questionnaire for headache diagnosis has been tested in China and used in epidemiological investigations of nationwide demographic headache (11–13). VAS scores have been shown to have high reliability, with an intraclass correlation coefficient of 0.97 (14). In this questionnaire, headache disorders included migraine, tension-type headache (TTH), and other types such as neuralgia, chronic daily headache, and unclassified headaches. Trigeminal autonomic cephalalgias, other primary headache disorders, and secondary headaches were not included.

D. The Pittsburg Sleep Quality Index (PSQI) uses 18 self-rated items to evaluate seven dimensions of sleep. Each dimension is scored on a scale of 0 to 3, and the total PSQI score for each dimension ranges from 0 to 21. The PSQI scores ranged from 0–5 for normal sleep, 6–10 for mild sleep disorders, 11–15 for moderate sleep disorders, and 16–21 for severe sleep disorders. In most studies, the Cronbach's alpha coefficient of the PSQI score was between 0.70 and 0.83, showing good internal consistency (15).

2.3. Statistical analysis

Epidata 3.1 was used for data entry, and statistical analyses were performed using SPSS version 26.0. The Kolmogorov–Smirnov test was used to examine the normality of the distribution of continuous variables. Data are expressed as mean (standard deviation) for normally distributed variables or median (interquartile range) for non-normally distributed variables, and categorical variables are summarized as the number and percentage.

Depression, anxiety, headache, and sleep disorders were defined as binary variables. Two subcategories of headache, migraines, and TTH were used as variables. The Chi-square test (categorical variables) and the Mann–Whitney U test (quantitative variables with non-normal distribution) were applied to compared the demographic information of the two groups of individuals with or without depression. Because there were ordinal categorical variables such as professional titles in the demographic data, we used a nonparametric Spearman correlation analysis for depression occurrence (binary variable). Considering that SDS scores are continuous variables that do not conform to a normal distribution, Spearman correlation analysis was also used, and Spearman's correlation coefficient (Spearman's rho) was calculated. The statistical significance level was set at $p < 0.05$.

Univariate logistic regression analysis was used to identify odds ratios (OR) and 95% confidence intervals according to demographic and occupational characteristics, anxiety, headache type, and sleep disorders. The independent variables with a p-value <0.10 by univariate logistic regression screening were included in the candidate variables of the multiple logistic regression model to predict the occurrence of depression. And multiple linear regression was also used to predict depression SDS scores.

3. Results

A total of 645 medical staff members (280 physicians and 365 nurses) were invited to participate in the study, of whom 22 refused to complete the survey. Another 75 participants either did not answer the questionnaire completely or did not meet the response requirements, with a correct response rate of 85%. A total of 548 respondents (240 doctors and 308 nurses) completed the survey. There were 144 men and 404 women, aged between 20 and 60 years, with a mean age of 30.5 ± 7.2. Of the 240 doctors, 138 were men and 102 were women. There were 6 men and 302 women among the 308 nurses.

3.1. Prevalence of depression, anxiety, headache, and sleep disorders

Among the 548 medical staff members, the 1-year prevalence of depression was 42.7% (mild, 26.8%; moderate and severe, 15.9%), the prevalence of headache disorders was 53.3% (migraine, 25.9%; TTH, 24.1%; other types, 3.3%), and the prevalence of anxiety and sleep disorders was 26.6% and 69.0%, respectively (see Figure 1). Among them, the prevalence of depression combined with anxiety, headache, and sleep disorders was 23, 27% (migraine 14.4%, TTH 10.4%), and 34.5%, respectively; the proportions of patients with depression with anxiety, sleep disorder, migraine, and TTH were 86.3%, 50%, 55.6%, and 43.2%, respectively (see Figure 2), but only 11 respondents (4.7%) had received psychiatric medication for depression.

We found that the prevalence of depression in women was significantly higher than in men (48.3% vs. 27.1%, OR = 2.512), and women were approximately five times as likely to have depression as males were (35.6% vs. 7.1%). The median age in the depressed group (28 years) was lower than that in the non-depressed group (30 years). The prevalence of depression in unmarried or divorced individuals was significantly higher than that in married individuals (50.5% vs. 35.8%, OR = 1.900). The prevalence of depression among nurses was nearly twice as high as that among doctors (55.2% vs. 26.7%, OR = 3.388), and was significantly higher among rotating-shift workers than among day-shift workers (35.2% vs. 7.5%, OR = 1.719). The total prevalence of overweight and obesity in the medical population was approximately 33.1%, among which 10.6% were depressed and 32.1% were depressed in the population with a BMI <23 kg/m^2. In addition, with improvements in educational backgrounds and professional titles, the prevalence of depression gradually decreased.

The prevalence of mild, moderate, and severe anxiety was higher in patients with depression than in those without. The prevalence of migraine was higher in the depressive group (55.6% vs. 44.4%, OR = 2.031), whereas the prevalence of TTH was higher in the non-depressive group (43.2% vs. 56.8%). In comparison with the sleep disorder group, we found that the prevalence of mild sleep disorders was similar in the two groups, while the prevalence of moderate and severe sleep disorders was higher in the depressive group. Table 1 presents the results of the study.

3.2. Correlation analysis and multiple logistic regression of the occurrence of depression

We first used nonparametric Spearman correlation analysis of the binary classification variables of depression and anxiety, headache, and sleep disorders, and then examined their association with demographic characteristic factors. The results showed that depression

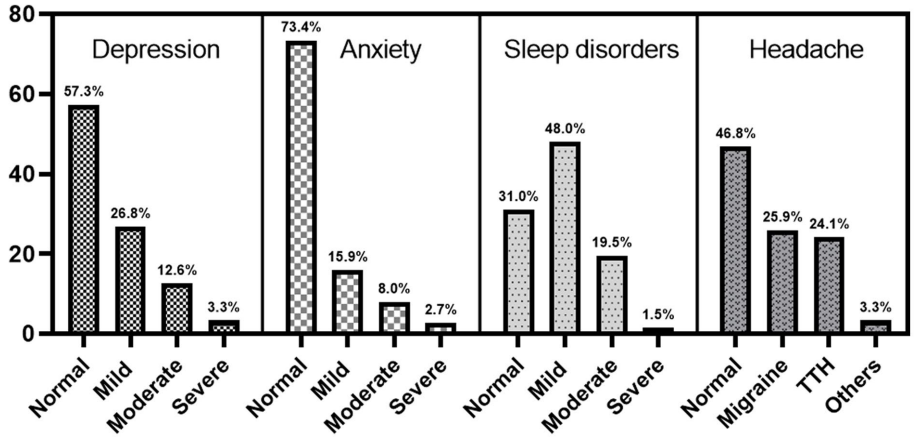


FIGURE 1
Prevalence of depression, anxiety, headache, and sleep disorders among 548 medical staff.

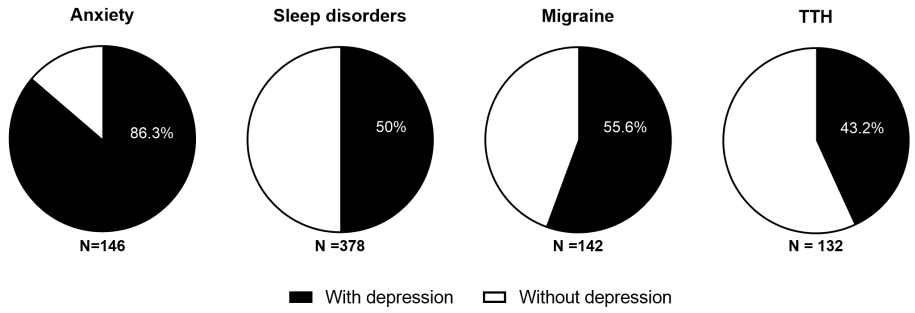


FIGURE 2
Proportion of patients with depression in anxiety, sleep disorder, migraine, and TTH.

was associated with anxiety, sleep disorders, total headache, and migraines, with the largest correlation coefficient for anxiety (Spearman's rho = 0.531). However, no significant association was observed between TTH levels and depression. Other related factors included age, sex, BMI, professional title, educational background, marital status, occupation, work arrangements, and night shifts (Figure 3A).

We performed a multifactor binary logistic regression analysis of the occurrence of depression. The TTH, headache frequency, and VAS scores for headache intensity were found have p-values >0.1 as determined by univariate logistic regression; therefore, they were not included in the multifactor regression model. The results showed that anxiety and nursing occupation were risk factors, whereas BMI was a protective factor against depression (Figure 4). The predictive accuracy of the multifactor binary logistic regression model was 78.5%.

3.3. Correlation analysis and multiple linear regression of depression SDS scores

We further analyzed the correlation between SDS scores for depression severity and the quantitative variables of SAS, PSQI, headache frequency, headache intensity, VAS scores, and demographic data. The results showed that the severity of depression was significantly correlated with the grades of anxiety and sleep disorders (Spearman's rho = 0.801, 0.503) and the presence or absence of headaches and migraines. However, there was no significant correlation between SDS scores and headache frequency, headache intensity, or TTH; however, headache frequency and headache intensity affected the PSQI score of sleep disorders (Spearman's rho = 0.205, 0.166, $p < 0.001$). In addition, the results showed that the severity of depression was positively correlated with nurse occupation, night shifts, and working arrangements, and negatively correlated with age, sex, marital status, BMI, educational background, and professional titles (see Figure 3B).

We then performed a multiple linear regression analysis of the SDS scores to predict depression severity. The VAS scores for headache intensity were found to have a p-value >0.1 in the early screening process; therefore, they were not included in the regression model. Considering the multicollinearity between age, working years, professional title, medical profession, sex, working arrangement, and night shift frequency, we only included variables such as age, nurse occupation, and night shift frequency. According to the results of the multiple linear regression analysis, grades of anxiety, sleep disorders, and nursing occupation were risk factors, while educational

TABLE 1 Comparison of the characteristics of medical staff with and without depression.

		With depression (*n* =234)	Without depression (*n* =314)	*P*-value	OR (95%CI)
Sex (*n*, %)	Male	39 (27.1%)	105 (72.9%)	<0.001[a]	0.398 (0.263–0.604)
	Female	195 (48.3%)	209 (51.7%)		
Age	Mean (±SD)	28.8 (±5.7)	31.7 (±8.0)	<0.001[b]	1.833 (1.302–2.582)
Marital status	Single or divorced	129 (51.2%)	126 (48.8%)	<0.001[a]	1.900 (1.348–2.678)
	Married	105 (35.6%)	188 (64.4%)		
BMI (kg/m^2)	Underweight <18.5	51 (56.0%)	40 (44.0%)	0.001[a]	
	Normal weight 18.5–22.9	125 (45.5%)	150 (54.5%)		
	Overweight 23–25	26 (31.3%)	57 (68.7%)		
	Obese ≥25	32 (32.3%)	67 (67.7%)		
Occupation	Doctor	64 (26.7%)	176 (73.3%)	<0.001[a]	0.295 (0.205–0.425)
	Nurse	170 (55.2%)	138 (44.8%)		
Educational background	College or lower	101 (54.6%)	84 (45.4%)	<0.001[a]	1.716 (1.186–2.483)
	Bachelor	124 (41.2%)	177 (58.8%)		4.126 (1.963–8.673)
	Masters or above	9 (14.5%)	53 (85.5%)		
Work Seniority (years)	Median (P25, P75)	5 (3,8)	6 (3,12)	0.021[b]	
Work arrangements	Dayshift	41 (32.8%)	84 (67.2%)	0.011[a]	0.582 (0.382–0.885)
	Rotating shift	193 (45.6%)	230 (54.4%)		
Night shifts	Median (P25, P75)	5 (4,8)	5 (0,7)	0.003[b]	
Professional titles	Junior	199 (48.8%)	209 (51.2%)	<0.001[a]	2.698 (1.629–4.467)
	Senior	24 (26.1%)	68 (73.9%)		1.187 (0.524–2.691)
	Advanced	11 (8.8%)	37 (77.1%)		
Anxiety	Total	126 (86.3%)	20 (13.7%)	<0.001[a]	17.150 (10.188–28.869)
	Mild	69 (79.3%)	18 (20.7%)		
	Moderate	42 (95.5%)	2 (4.5%)		
	Severe	15 (100%)	0		
Headache	Total	148 (50.7%)	144 (49.3%)	<0.001[a]	
	Migraine	79 (55.6%)	63 (44.4%)		2.032 (1.437–2.872)
	Tension-type headache	57 (43.2%)	75 (56.8%)		
Sleep disorders	Total	189 (50.0%)	189 (50.0%)	<0.001[a]	
	Mild	104 (39.5%)	159 (60.5%)		2.778 (1.870–4.127)
	Moderate	77 (72.0%)	30 (28.0%)		
	Severe	8 (100%)	0		

[a]Chi-squared test.
[b]Mann-Whitney U test. OR, odds ratio; CI, confidence interval; SD, standard deviation; BMI, body mass index.

background was a protective factor against depression severity (see Figure 5).

4. Discussion

4.1. Prevalence

The prevalence of depression in the medical population was significantly higher than that in the general population, particularly among women and nurses. The estimated prevalence of depression among resident doctors in a systematic review published in 2015 was 28.8%, ranging from 20.9 to 43.2%, depending on the assessment tools used (16). Many studies have reported that the prevalence of depression among nurses ranges from 18 to 64.8% (17–21), and some studies have suggested that the prevalence of depression among nurses is nearly twice that among other professional individuals (22). The prevalence of depressive symptoms among Chinese nurses between 1996 and 2019 was approximately 43.8% (23). In our study, the prevalence of depression among physicians and nurses was 26.7% and 55.2%, respectively, which is consistent with the results of previous reports and indicates that the mental health of nurses requires more attention from society.

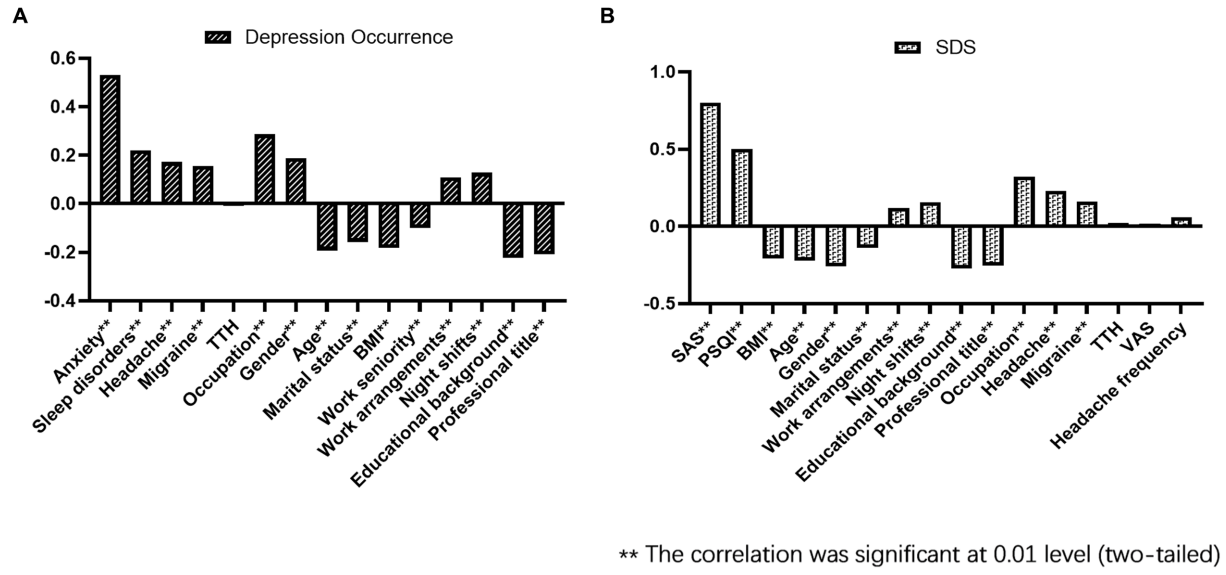
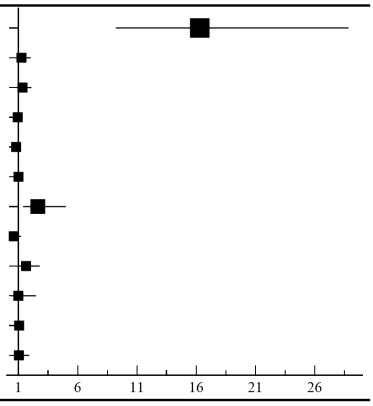


FIGURE 3
Nonparametric Spearman correlation analysis of depression occurrence **(A)** and SDS **(B)**.

Risk factor	P-value	OR(95%CI)
Anxiety	<0.001**	16.298(9.208~28.847)
Sleep disorders	<0.360	1.256(0.772~2.043)
Headache	0.212	1.331(0.850~2.085)
BMI	0.032*	0.925(0.861~0.993)
Education background	0.250	0.797(0.543~1.172)
Age	0.962	0.999(0.942~1.058)
Nurse occupation	0.003**	2.626(1.381~4.993)
Gender	0.153	0.603(0.301~1.206)
Marital status	0.076	1.627(0.950~2.785)
Work arrangements	0.956	0.974(0.383~2.479)
Night shifts	0.467	1.046(0.927~1.180)
Professional title	0.926	1.029(0.560~1.893)



** The correlation was significant at 0.01 level (two-tailed)

FIGURE 4
Odds ratio (ORs) forest plot of multiple logistic regression for depression occurrence.

4.2. Anxiety and depression

The occurrence of depression was correlated with anxiety, sleep disorders, headache, and migraine, among which the correlation with anxiety was the strongest. Previous studies have consistently identified risk factors for depression, including cognitive and cognitive processes, stressors, sociodemographic factors (e.g., being female), parental depression, and certain behaviors and personalities. Stress is a risk factor for depression, and more than 80% of the individuals in the community sample who met the criteria for clinically significant depression had experienced a recent major life event or persistent stressor. These risks and depression interact in a bidirectional and dynamic manner (24). Medical staff face multiple stressors from patients, society, family, and individuals, which often leads to anxiety. Anxiety disorders usually first appear in early childhood and adolescence, long before depression develops, and 56% of individuals with anxiety disorders develop depression. Anxiety disorders can be described as risk factors for secondary depression in this age group (25). Our study found that anxiety was significantly correlated with the occurrence and severity of depression, and that stress may be the dominant factor. Changes in neurobiological substrates related to stress regulation and maladjustment of transmitter activity are possible mechanisms underlying anxiety and depression (26). We also found that the higher the educational level, the lower the prevalence and severity of depression. This is because people with different degrees have different levels of self-regulation and cognitive abilities to cope with stress, and many studies have shown that highly educated adults have lower levels of depression. Therefore, we believe that there is a cognition-stress-anxiety-depression relationship.

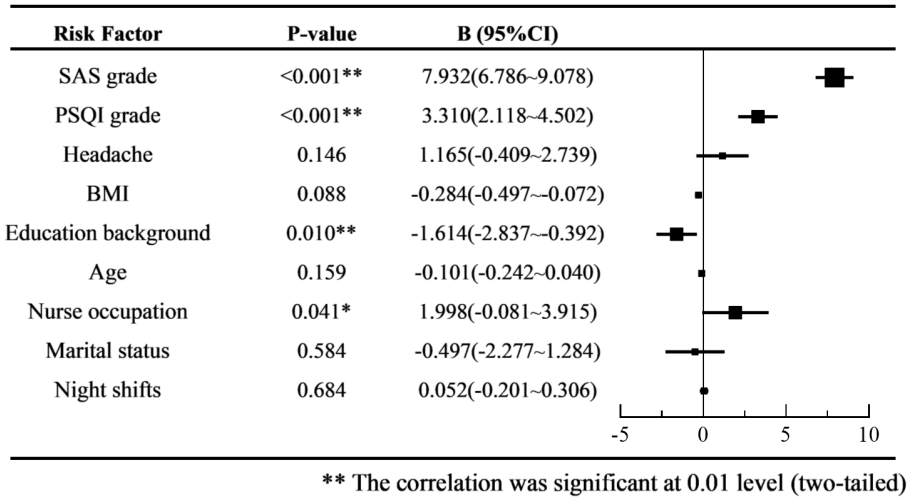


FIGURE 5
Forest plot of multiple linear regression coefficient B of SDS score.

4.3. Headache and depression

Our survey found that the occurrence of depression was associated with the presence or absence of headache or migraine, but there was no significant correlation between the severity of depression and the severity score of headache, which is consistent with previous reports (27). There was a bidirectional association between headache and depression, with patients with depression having an increased risk of migraine, and migraineurs having an increased risk of depression. Moreover, the symptoms of migraine and depression are more severe than those who suffer alone (28, 29). Headache frequency has also been reported to affect depression scores (30). In our study, no significant difference in TTH was found between groups with and without depression, which differs from the results of a general population sample (31). There is little epidemiological data on TTH among medical staff. The reasons for this difference are related to the characteristics and working modes of medical staff, among whom TTH is more likely to be induced by long-term desk work and frequent night shifts.

4.4. Sleep disorders and depression

In our survey, sleep disorders were significantly associated with the occurrence and severity of depression. It is currently believed that the relationship between depression and sleep disorders is reciprocal. A longitudinal study showed that both anxiety and depression are significantly linked to the incidence, but not persistence, of sleep disorders (32). Studies have also identified sleep disorders as an independent risk factor for the onset or recurrence of depression in young, middle-aged, and older adults (33, 34). Moreover, one of the symptoms most consistent with major depressive disorder is sleep disturbance (35). In addition, patients with depression and sleep disorders tended to have more severe depressive symptoms, longer treatment times, and lower remission rates (36). Therefore, more attention should be paid to sleep disorder interventions when treating depression.

4.5. BMI and depression

There have been many studies on the relationship between depression and BMI, but consistency has been poor. There is a range from negative correlation studies (37–41) on "happy obesity" to positive correlation studies (42, 43), and there are also studies showing that the correlation between BMI and depression can be ignored (44). Our results showed that BMI was negatively associated with depression, although the correlation coefficient was small. The reason for this may be that different ages, sexes, and educational backgrounds have different body shape cognitions. Further stratified research on the relationship between BMI and depression is required.

4.6. Limitations

In terms of limitations, our study relied on the participants' memories, and recall bias may have affected the reliability of the survey data. Moreover, only one assessment tool was used for each disease, which is another limitation of this study. Multiple assessment tools and objective examinations can be combined to refine the stressors in the medical population for further analysis. Further, as a cross-sectional study, we found associations between depression, anxiety, headache, and sleep disorders, but could not disentangle the cause and effect. It is well known that genetic factors play an important role in the development of depression, but family history of depression and other factors such as alcohol use and sun exposure time were not included in our survey, which should be explored in future studies.

5. Conclusion

Overall, emotional disorders such as depression are more prevalent in the healthcare population, especially among women and nurses, but they rarely attract attention and lack effective treatment. Depression, anxiety, headache, and sleep disorders often co-occur and interact with each other. Assessment of mood, headache, and sleep

problems is of great significance for more effective prevention and treatment of depression among medical staff.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the ethics committee of the Chinese PLA General Hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

GL was responsible for reviewing the literature and writing the manuscript. SX was responsible for the data analysis. WX and WG provided the raw data and guidance. JH, FM, and YY were responsible for issuing and recalling the SDS/SAS/PSQI questionnaires. RL and SY were the principal investigators responsible for the study design, data analysis and interpretation, manuscript revision, had full access to all data in the study, and had the final responsibility for the decision to submit the manuscript for publication. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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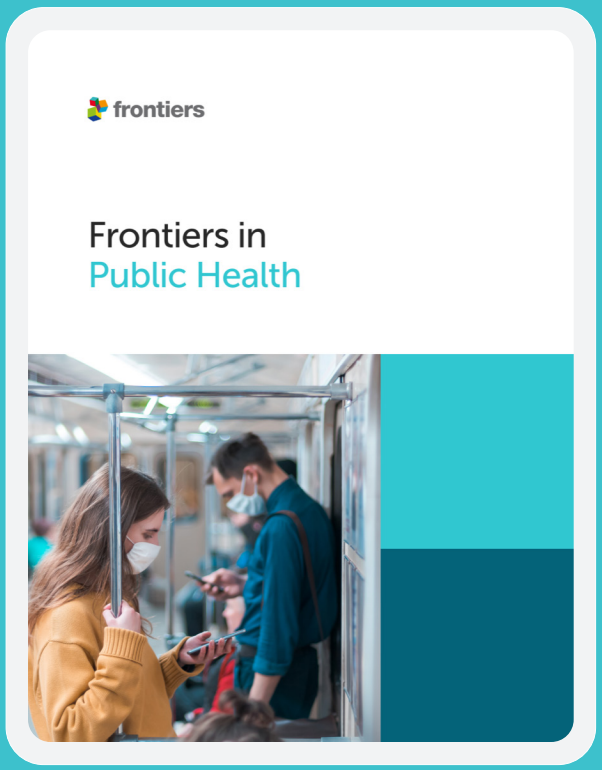

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