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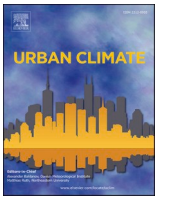

Urban heat island and the risk of schizophrenia spectrum disorders in middle-aged and older adults

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ABSTRACT

Rapid urbanization and climate crisis amplified the adverse effects of urban heat, while it remained unclear about the long-term impacts of urban heat island (UHI) on mental disorders, especially schizophrenia spectrum disorders (SSD). This study included 393,507 participants from the UK Biobank to examine the impact of long-term exposure to UHI on the incidence risk of SSD and changes of brain structures. UHI exposure were quantified as surface UHI intensity and normalized land surface temperature from satellite data. Cox proportional hazard models and multiple linear regression models were used to examine associations of UHI effects with SSD and changes of brain structures. During a median follow-up of 13.8 years, there were 1112 (0.3 %) participants diagnosed with SSD and 367 (0.1 %) with schizophrenia. Every standard deviation increased surface UHI intensity was associated with a 17 % (HR, 1.17; [95 % CI, 1.07–1.28]) excess risk of SSD and a 26 % excess risk of schizophrenia (HR, 1.26; [95 % CI, 1.08–1.46]). These effects were more pronounced in individuals with a high genetic risk of schizophrenia and those aged <60 years. UHI exposure was also associated with brain macrostructure and microstructure, particularly in the frontal and temporal lobes, as well as white matter tracts. In this cohort study of middle-aged and older adults, UHI exposure was identified as a risk factor for the onset of SSD and schizophrenia. These findings highlight the need for implementing initiatives of UHI mitigation and heat resilience to improve mental health and sustainable development in urban communities worldwide.

1. Introduction

Consensus has been reached that the world is facing an incredible climate crisis (Mitchell, 2021). From 2000 to 2019, there were approximately 489,000 annual heat-related deaths and the risk was projected to further elevate due to enhanced global warming

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(Howard et al., 2024; Khatana et al., 2024; Luthi et al., 2023; Wu et al., 2022). Aging and rapid urbanization increase the susceptibility of the population to the adverse effects of urban heat (Falchetta et al., 2024; Xi et al., 2024). Many densely populated cities were poorly designed to mitigate the accumulation and generation of urban heat, with excess heat being further exacerbated by reduced green space, unsuitable building materials, and massive anthropogenic heat emissions (Nieuwenhuijsen, 2021; Tong et al., 2021).

Recent evidence showed that exposure to urban heat island (UHI), characterized by elevated temperatures concentrated in urban centers and a declining thermal gradient extending toward their neighboring rural counterparts, was negatively associated with human well-being (Hsu et al., 2021). Meanwhile, the intricate relationship between extreme heat and mental health has come under intense scrutiny, with documented associations between short-term exposure to extreme heat and elevated risks of hospitalization for mental illnesses (Cloud et al., 2023; Crandon et al., 2022; Cuijpers et al., 2023; Lawrance et al., 2022; Li et al., 2023; Liu et al., 2021; Nori-Sarma et al., 2022). The underlying mechanisms include alteration of internal biochemical levels, disruption of thermoregulatory homeostasis, break of thermosensitivity, and diverse social and cultural factors (Cramer et al., 2022; White, 2024). However, the long-term impact of UHI exposure on mental well-being, particularly in schizophrenia spectrum disorders (SSD), has yet to be thoroughly investigated, resulting in unclear targets and interventions for enhancing heat resilience in the general and vulnerable populations.

To narrow the gaps, this study, leveraging the UK Biobank's longitudinal health data, aimed to estimate the potential long-term effects of UHI exposure on the incidence risk of SSD across subgroups with diverse genetic predispositions of schizophrenia. This study also estimated the adverse heat effects on the brain microstructural traits relevant to SSD. The findings would provide epidemiological evidence to understand the urban heat problem, identify vulnerable populations, and inform policymakers on the need to take immediate actions for the development of heat-resilient cities, promotion of urban sustainability, and enhancement of public mental well-being.

2. Methods

2.1. Study population

The study adopted data from the UK Biobank under application number 99001. The UK Biobank is an ongoing community-based

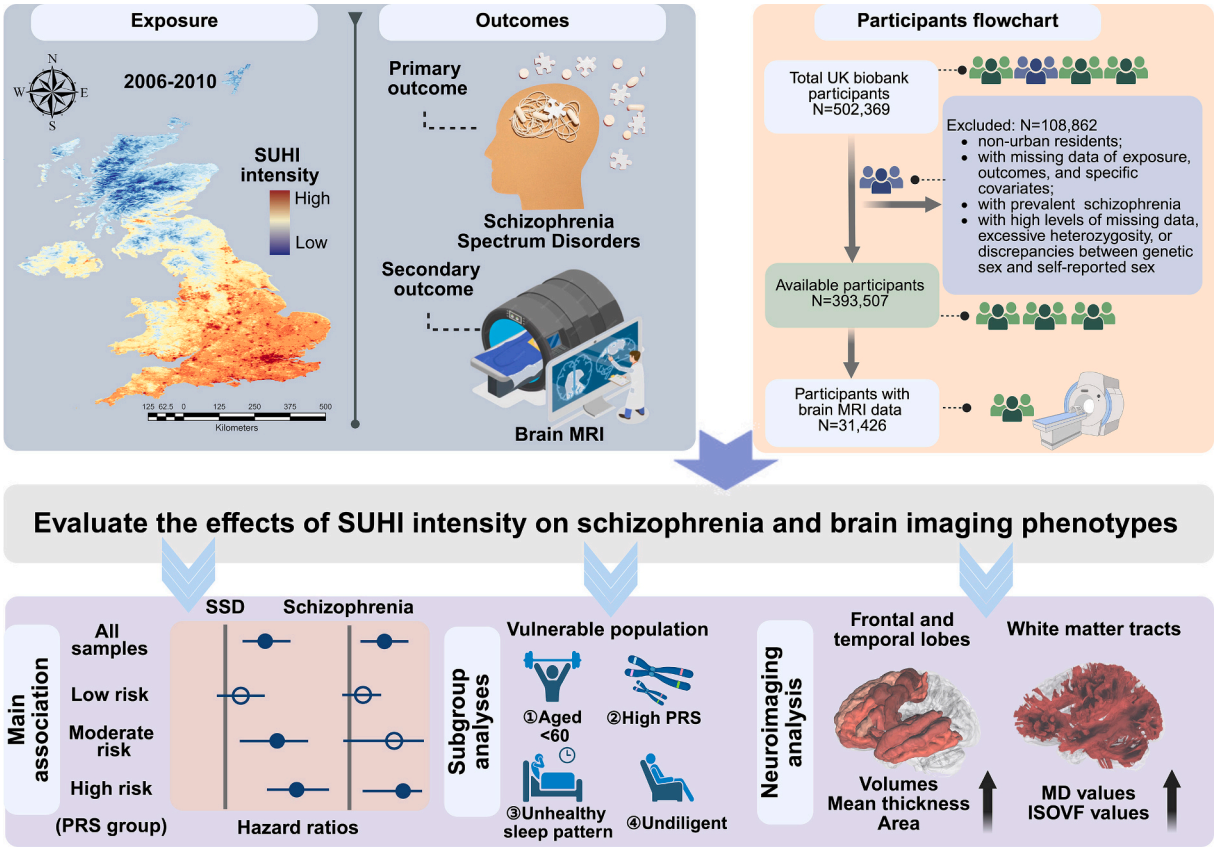

Fig. 1. Study workflow. Top left: the distribution of SUHI intensity in the UK at baseline (2006–2010), and the primary and secondary outcomes in this study. Top right: participant flowchart in the analysis. Bottom: the main and subgroup associations of SUHI intensity with SSD and schizophrenia; relationships of SUHI intensity with brain grey and white matter.

prospective cohort study with over 500,000 million adults aged 39–73 years recruited during 2006–2010. At baseline, all participants completed touchscreen questionnaires, physical examinations, blood sample collections, and other assessments at 22 assessment centers across England, Wales, and Scotland. Since 2014, participants were reinvited to take brain Magnetic Resonance Imaging (MRI) assessments. The UK Biobank study received ethical approval from the North West Multi-center Research Ethics Committee. All participants had provided written informed consent. After excluding non-urban residents, individuals with missing data, elevated heterozygosity, or inconsistent data, and those with prevalent SSD, a total of 393,507 urban residents were included (Fig. 1). Reporting of the study followed the Strengthening the Reporting of Observational Studies in Epidemiology guideline.

2.2. Assessment of exposure

The study utilized the satellite data of the Moderate Resolution Imaging Spectroradiometer (MODIS) land surface temperature (LST) product as the data source. The MYD11A2 product from Terra MODIS images provided an eight-day averaged LST with a 1000 m spatial resolution by a split-window algorithm with cloud removal, atmospheric water vapor, radiation, and temperature correction (Wan, 2008). Retrieval of high-quality LST data depends on clear-sky conditions, while clouded or rainy skies may lead to notable gaps or missing values. Despite such unresolved gaps for satellite data, the quality of MODIS products has been well acknowledged in the identification of surface thermal characteristics (Wan, 2008). To determine the division between urban and non-urban areas, the Land Cover Type Yearly Global 500 m product (MCD12Q1, derived by supervised classifications of MODIS Terra and Aqua reflectance data) was employed (Friedl et al., 2010). We categorized the land types of the study area into urban, non-urban, and water bodies at baseline according to the land cover map (17–class University of Maryland scheme).

The study adopted surface UHI (SUHI) intensity and normalized LST as the UHI effect. For the two indices, we calculated the mean value at baseline (2006–2010) and annual mean values from 2006 to 2022, respectively. The SUHI intensity was computed by the difference in mean daytime LST between urban and non-urban areas, and was then normalized. The normalized LST was calculated as the difference between the daytime LST value and the average daytime LST value of the study area, and then divided by the standard deviation (SD). The two indices were further averaged in 500 m buffers based on the residential coordinate as the UHI exposure value of each participant.

2.3. Ascertainment of outcomes

The primary outcomes were incident SSD (International Classification of Disease-10, ICD-10: F20-F29) and schizophrenia (ICD-10: F20). Hospitalization data from national health registers across England, Scotland, and Wales, was utilized to identify the date of disease onset. The follow-up was from the date of baseline assessment until the date of death, diagnosis, loss to follow-up, or 19th Dec 2022, whichever came first.

The secondary outcomes were brain imaging phenotypes measured by brain MRI since 2014. The measurement was used by the Siemens Skyra 3 T scanner with a standard Siemens 32-channel RF receiver head coil. The MRI data was processed by the UK Biobank through FreeSufer and available as image-derived phenotypes (IDP). In this study, IDPs included SSD-related 42 cortical regions (26 in the frontal lobe and 16 in the temporal lobe) (Jauhar et al., 2022), extracted from FreeSurfer desikan white (Category ID: 192). The volumes, mean thickness, and areas of these regions were selected. Diffusion MRI data was processed to extract quantitative metrics related to brain microstructure. Preprocessing included corrections for eddy currents, head motion, and geometric distortions using the FSL Eddy tool and subsequent geometric distortion correction in corrected 4D data. The data (Category ID: 135) was analyzed using diffusion tensor imaging and Neurite Orientation Dispersion and Density Imaging models. This study focused on mean diffusivity (MD) and isotropic volume fraction (ISOVF) of 27 white matter tracts since they were closely related to brain edema, and the latter was a known consequence of heat exposure (White, 2024). Details on data processing can be found at https://biobank.ctsu.ox.ac.uk/crystal/crystal/docs/brain_mri.pdf. All brain phenotypes were normalized as z-scores for head size and the values were naturally log-transformed when not normally distributed. Field identifications of the brain structures in the study are described in supplemental eTable 1.

2.4. Covariates

We selected sociodemographic factors (age, sex, education, income, ethnicity, and Indices of Multiple Deprivation [IMD]), waist-hip ratio (WHR), healthy lifestyle (never smoking, moderate drinking, regular physical activity, healthy sleep pattern, and healthy diet), and comorbidities (hypertension, diabetes, and coronary artery disease) from the baseline assessment of UK Biobank dataset as potential confounding factors (Bao et al., 2024; Chen et al., 2024; Hu et al., 2024). Income was classified into low and high levels by the median (£31,000). IMD quantified a variety of social deprivation components with a single value, including income, employment, education, health, crime, and other themes. The calculation of the genetic risk of schizophrenia by polygenic risk score (PRS), and the definition on the levels of education, personality, social isolation, and loneliness can be found in supplemental eMethods and eTable 2.

2.5. Statistical analysis

The baseline characteristics were summarized as the median (interquartile range, IQR) for continuous variables and counts (percentage) for categorical variables. Both time-independent and time-dependent Cox proportional hazard regression models were performed. The strength of each association was presented as a hazard ratio (HR) together with its 95 % confidence interval (CI). The

exposure was treated as the continuous variable (every SD) and categorical variable (low and high levels based on the median at baseline [normalized LST: 1.37, SUHI intensity: 3.44 °C], with the low level as the reference). The proportional hazard assumption was verified through the Schoenfeld residuals, and no violations were observed. The regression models were adjusted for age, sex, education, income, IMD, ethnicity, WHR, healthy lifestyle, and prevalent diseases. The potential interplay between UHI exposure and genetic susceptibility was investigated by relative excess risk due to interaction (RERI) and 95 % CI. A natural cubic spline regression model was employed to assess the non-linear relationship between UHI exposure and SSD with three degrees of freedom.

To assess the modifying effects of covariates, we conducted stratified analyses by binary factors of age, sex, social isolation, loneliness, warmth, diligence, nervousness, sociability, curiosity, regular physical activity, healthy sleep pattern, and healthy diet. The *P* for interaction was evaluated using a multiplicative scale, whereby a product term was incorporated into the model to test the statistical significance of heterogeneity. Multiple linear regression models were used to identify the effect of UHI on brain structures. The results were presented as *β*s and 95 % CIs. We applied false discovery rates (FDR) correction to reduce the false positives arising from multiple tests.

Several sensitivity analyses were performed to verify the robustness of the results. First, we excluded the non-Whites due to the high proportion of the Whites (about 97 %). Second, we removed exposure outliers (≥99th percentile) to minimize the extreme effect. Third, we advanced the follow-up to December 31, 2019, to avoid the impact of COVID-19 (Han et al., 2023). Fourth, we used average normalized LST and SUHI intensity in buffers of 300 m as exposure. Last, we controlled social isolation and loneliness in the model. All analyses were performed using the R software, version 4.2.2. The level of statistical significance was determined to be $P < 0.05$.

3. Results

Among 393,507 participants, there were 224,253 (57.0 %) participants aged less than 60 years and 213,257 (54.2 %) were females. During a median follow-up of 13.8 years, there were 1112 (0.3 %) participants diagnosed with SSD and 367 (0.1 %) were schizophrenia. Participants exposed to high-level SUHI intensity were more likely to be younger (<60 years, 58.9 % vs 55.1 %), with lower IMD (median, 14.7 vs 11.9), poor WHR (49.4 % vs 48.7 %), never smoking (53.2 % vs 55.5 %), and more prevalent with diabetes (5.7 % vs 4.9 %), compared to those with lower SUHI intensity (supplemental eTable 3–4).

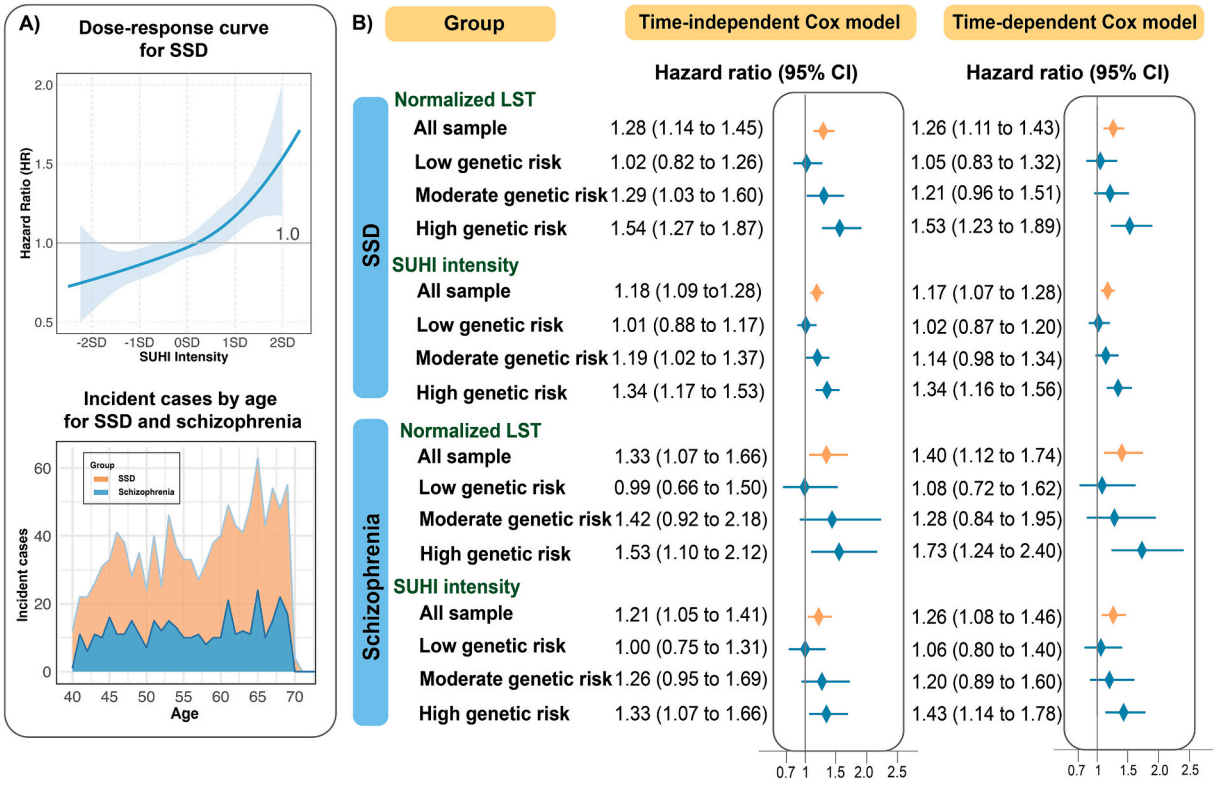

Fig. 2. Associations of normalized LST and SUHI intensity with incidence risks of SSD and schizophrenia by genetic risks. **A)** Dose-response curve of SSD and the incident cases of SSD and schizophrenia by age in the UK. **B)** A total of 393,507 participants were utilized to assess the relationship of UHI exposure (normalized LST and SUHI intensity) with SSD and schizophrenia by genetic risks. Normalized LST and SUHI intensity were analyzed as the continuous variable (every SD). The genetic risks were classified into low (tertile 1), moderate (tertile 2), and high (tertile 3) according to the distribution. Both time-independent and time-dependent Cox proportional hazard models were adjusted for age, sex, education, income, IMD, ethnicity, WHR, healthy lifestyle, and prevalent diseases.

During the follow-up, urban heat hot spots were mainly distributed in cities like London, and Manchester (supplemental eFigure 1). There were 653 (58.7 %) and 225 (61.3 %) participants with new-onset SSD and schizophrenia exposed to higher SUHI intensity. After adjusting for potential confounders in the time-dependent models, every SD increase in SUHI intensity was positively associated with a 17 % excess risk of SSD (HR, 1.17; [95 % CI, 1.07–1.28]) and a 26 % excess risk of schizophrenia (HR, 1.26; [95 % CI, 1.08–1.46]) (Fig. 2 and supplemental eFigure 2). Pronounced associations were observed among individuals with high PRS of schizophrenia, with HRs of 1.34 (95 % CI, 1.16–1.56) for SSD and 1.43 (95 % CI, 1.14–1.78) for schizophrenia. Consistently addictive interaction effects were also found among the high PRS group, with RERIs of 0.52 (95 % CI, 0.10–0.92) for SSD (Table 1). Similar findings were observed for the exposure as categorical variables (supplemental eTable 5).

Stratification analysis by the time-dependent models showed that younger adults ($HR_{SUHI\ intensity}$, 1.50; [95 % CI, 1.23–1.82]) were more vulnerable to schizophrenia than adults over 60 years ($HR_{SUHI\ intensity}$, 0.99; [95 % CI, 0.79–1.24]) (*P* for interaction = 0.005). Participants without diligence were more vulnerable to developing SSD ($HR_{SUHI\ intensity}$, 1.29; [95 % CI, 1.14–1.46] vs $HR_{SUHI\ intensity}$, 1.04; [95 % CI, 0.91–1.19], *P* for interaction = 0.020) and schizophrenia ($HR_{SUHI\ intensity}$, 1.41; [95 % CI, 1.15–1.73] vs $HR_{SUHI\ intensity}$, 1.01; [95 % CI, 0.79–1.29], *P* for interaction = 0.033) compared with their counterparts. For healthy lifestyle, the effect sizes for the associations of SUHI intensity with SSD (HR, 1.29; [95 % CI, 1.16–1.44] vs HR, 1.07; [95 % CI, 0.95–1.20], *P* for interaction = 0.017) and schizophrenia (HR, 1.51; [95 % CI, 1.24–1.84] vs HR, 0.92; [95 % CI, 0.74–1.14], *P* for interaction = 0.001) were generally larger in participants without healthy sleep patterns in the time-independent models (Table 2). The results by normalized LST showed consistent findings (supplemental eTable 6–7).

A sub-sample of 31,426 participants with brain MRI was retained for neuroimaging analyses. After covariate adjustments and FDR correction, every SD increase in SUHI intensity was positively associated with the MD and ISOVF values of white matter in the right hemisphere, especially for inferior longitudinal fasciculus tract (MD: β, 0.050; [95 % CI, 0.043–0.058]; ISOVF: β, 0.116; [95 % CI, 0.108–0.124]), inferior fronto-occipital fasciculus tract (MD: β, 0.041; [95 % CI, 0.034–0.048; ISOVF: β, 0.108; [95 % CI, 0.100–0.117]), and parahippocampal part of cingulum tract (MD: β, 0.037; [95 % CI, 0.029–0.045]; ISOVF: β, 0.055; [95 % CI, 0.047–0.063]) (Fig. 3 and supplemental eTable 8–9). Mild sex heterogeneities were found in several associations with brain macrostructure and microstructure (supplemental eTable 10–11). Sensitivity analyses demonstrated the robustness of the main results (supplemental eTable 12).

4. Discussion

The study showed that long-term exposure to UHI might have a significant impact on the onset of SSD and abnormalities of brain macrostructure and microstructures. The populations with a high genetic risk of schizophrenia and aged <60 years, were more vulnerable. The latent effect modification of specific personality traits was also observed. To our knowledge, this is one of the few studies indicating that UHI exposure could be an environmental stressor for SSD in urban contexts and the first study estimating the effects on SSD-related brain imaging phenotypes.

Schizophrenia, one of the most severe of all psychiatric illnesses, remains a huge etiological challenge. At present, it is widely accepted that both genetic and environmental factors appear to play a critical role in the initiation of schizophrenia (Jauhar et al., 2022). With the rising public concern about the risk of climate change to human health, climate-related factors, such as heat exposure,

Table 1
Interaction effect of urban heat island and genetic risk on the incidence of SSD and schizophrenia.

Group	HR (95 % CI)			RERI[c]	
	Low PRS[b]	Moderate PRS	High PRS	Moderate PRS	High PRS
SSD					
Normalized LST					
Low level	1.00	0.93 (0.70, 1.24)	0.99 (0.75, 1.32)	–	–
High level	1.17 (0.89, 1.54)	1.15 (0.87, 1.51)	1.68 (1.30, 2.17)	0.05 (−0.40, 0.44)	0.52 (0.10, 0.92)
SUHI intensity					
Low level	1.00	0.93 (0.70, 1.24)	0.99 (0.75, 1.32)	–	–
High level	1.17 (0.89, 1.54)	1.15 (0.87, 1.51)	1.68 (1.30, 2.17)	0.05 (−0.40, 0.44)	0.52 (0.10, 0.92)
Schizophrenia					
Normalized LST					
Low level	1.00	0.86 (0.50, 1.46)	1.20 (0.73, 1.97)	–	–
High level	1.05 (0.63, 1.76)	1.01 (0.50, 1.69)	1.92 (1.22, 3.01)	0.10 (−0.80, 0.76)	0.67 (−0.13, 1.41)
SUHI intensity					
Low level	1.00	0.86 (0.50, 1.46)	1.20 (0.73, 1.97)	–	–
High level	1.05 (0.63, 1.76)	1.01 (0.60, 1.69)	1.92 (1.22, 3.01)	0.10 (−0.80, 0.76)	0.67 (−0.13, 1.41)

Abbreviation: HR, hazard ratio; CI, confidence interval; PRS, polygenic risk score; RERI, relative excess risk due to interaction; LST, land surface temperature; SSD, schizophrenia spectrum disorders; SUHI, surface urban heat island. **a** The normalized LST and SUHI intensity were categorized into high and low levels based on the median. **b** The PRS score was classified into low (tertile 1), moderate (tertile 2), and high (tertile 3) according to the distribution. **c** To estimate the RERI, the low UHI exposure and the lowest genetic risk (low PRS) groups were the reference categories. **d** The *P*-values for multiplicative interaction were calculated using a multiplicative interaction term included in the Cox regression model.

Table 2
Subgroup analyses of SUHI intensity with SSD and schizophrenia.

Subgroup	SSD				Schizophrenia			
	Time-independent[a] (HR, 95 % CI)	*P* for interaction	Time-dependent[b] (HR, 95 % CI)	*P* for interaction	Time-independent[a] (HR, 95 % CI)	*P* for interaction	Time-dependent[b] (HR, 95 % CI)	*P* for interaction
Demographics								
Age								
<60	1.24 (1.11, 1.38)		1.24 (1.10, 1.40)		1.40 (1.16, 1.70)		1.50 (1.23, 1.82)	
≥60	1.11 (0.99, 1.26)	0.193	1.10 (0.97, 1.25)	0.167	0.99 (0.79, 1.24)	0.019	0.99 (0.79, 1.24)	0.005
Sex								
Female	1.15 (1.02, 1.29)		1.19 (1.05, 1.35)		1.15 (0.95, 1.39)		1.19 (0.98, 1.43)	
Male	1.22 (1.09, 1.36)	0.468	1.15 (1.02, 1.30)	0.696	1.31 (1.04, 1.65)	0.381	1.38 (1.09, 1.73)	0.312
Social loneliness								
Loneliness								
Yes	1.31 (1.00, 1.72)		1.38 (1.04, 1.84)		1.64 (1.05, 2.56)		1.71 (1.10, 2.66)	
No	1.16 (1.06, 1.26)	0.406	1.14 (1.04, 1.26)	0.218	1.18 (1.00, 1.39)	0.172	1.23 (1.05, 1.45)	0.167
Social isolation								
Yes	1.20 (1.03, 1.39)		1.22 (1.04, 1.43)		1.18 (0.95, 1.48)		1.25 (1.00, 1.56)	
No	1.15 (1.05, 1.27)	0.646	1.13 (1.02, 1.26)	0.451	1.16 (0.96, 1.40)	0.896	1.19 (0.98, 1.44)	0.735
Personality								
Warmth								
No	1.22 (1.06, 1.41)		1.26 (1.08, 1.46)		1.22 (0.99, 1.52)		1.36 (1.09, 1.68)	
Yes	1.16 (1.04, 1.29)	0.560	1.13 (1.01, 1.28)	0.265	1.24 (0.99, 1.54)	0.948	1.22 (0.98, 1.51)	0.478
Diligence								
No	1.22 (1.09, 1.37)		1.29 (1.14, 1.46)		1.30 (1.07, 1.59)		1.41 (1.15, 1.73)	
Yes	1.10 (0.97, 1.25)	0.229	1.04 (0.91, 1.19)	0.020	1.04 (0.82, 1.33)	0.155	1.01 (0.79, 1.29)	0.033
Nervousness								
No	1.11 (0.99, 1.25)		1.07 (0.95, 1.22)		1.21 (0.96, 1.52)		1.18 (0.94, 1.47)	
Yes	1.24 (1.09, 1.41)	0.229	1.27 (1.10, 1.46)	0.075	1.16 (0.95, 1.43)	0.798	1.28 (1.04, 1.57)	0.582
Sociability								
No	1.2 (1.07, 1.34)		1.20 (1.06, 1.36)		1.18 (0.97, 1.44)		1.26 (1.03, 1.54)	
Yes	1.12 (1.00, 1.26)	0.438	1.11 (0.98, 1.26)	0.408	1.13 (0.90, 1.43)	0.773	1.13 (0.90, 1.42)	0.472
Curiosity								
No	1.24 (1.12, 1.36)		1.16 (1.04, 1.30)		1.25 (1.05, 1.48)		1.29 (1.09, 1.54)	
Yes	1.01 (0.86, 1.18)	0.031	1.13 (0.95, 1.35)	0.789	1.18 (0.85, 1.64)	0.765	1.22 (0.88, 1.70)	0.765
Healthy lifestyle								
Regular physical activity								
Yes	1.16 (1.03, 1.30)		1.18 (1.04, 1.35)		1.23 (0.98, 1.55)		1.32 (1.06, 1.66)	
No	1.20 (1.08, 1.34)	0.661	1.16 (1.03, 1.31)	0.857	1.20 (0.99, 1.45)	0.848	1.21 (1.00, 1.47)	0.558
Healthy sleep pattern								
Yes	1.07 (0.95, 1.20)		1.08 (0.95, 1.22)		0.92 (0.74, 1.14)		0.97 (0.78, 1.21)	
No	1.29 (1.16, 1.44)	0.017	1.26 (1.12, 1.42)	0.064	1.51 (1.24, 1.84)	0.001	1.54 (1.26, 1.87)	0.002
Healthy diet								

(*continued on next page*)

Table 2 (*continued*)

Subgroup	SSD				Schizophrenia			
	Time-independent[a] (HR, 95 % CI)	*P* for interaction	Time-dependent[b] (HR, 95 % CI)	*P* for interaction	Time-independent[a] (HR, 95 % CI)	*P* for interaction	Time-dependent[b] (HR, 95 % CI)	*P* for interaction
Yes	1.04 (0.91, 1.19)		1.06 (0.92, 1.23)		1.12 (0.87, 1.43)		1.09 (0.85, 1.40)	
No	1.27 (1.15, 1.40)	0.017	1.24 (1.11, 1.39)	0.081	1.26 (1.06, 1.51)	0.432	1.35 (1.13, 1.62)	0.157

Abbreviation: SSD, schizophrenia spectrum disorders; SUHI, surface urban heat island. **a** Time-independent (exposure at baseline period) cox proportional hazard model was utilized to estimate the association of normalized LST with SSD and schizophrenia with HRs and corresponding 95 % CI. **b** Time-dependent (exposure from 2006 to 2022) cox proportional hazard model was utilized to estimate the association of normalized LST with SSD and schizophrenia with HRs and corresponding 95 % CI.

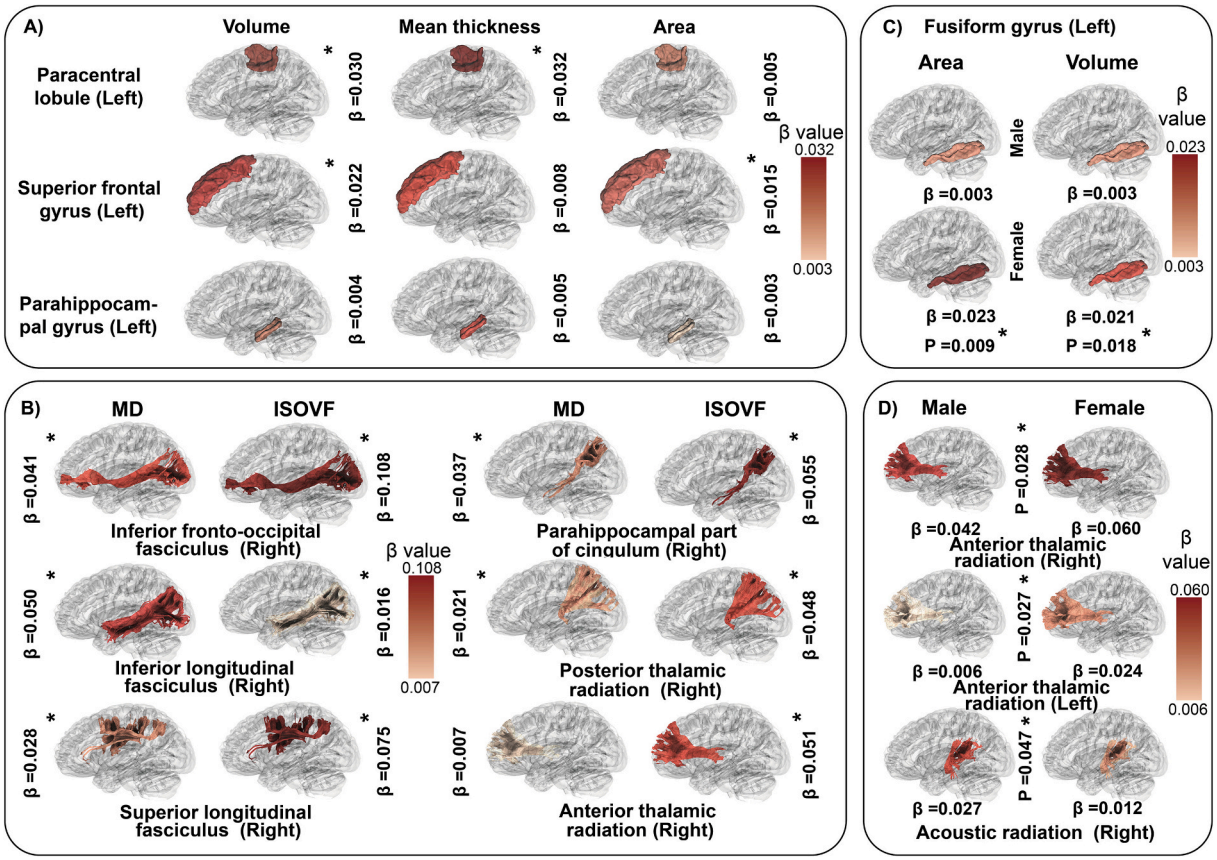

Fig. 3. Associations of SUHI intensity with the phenotypes of grey and white matter. **A)** The associations of SUHI intensity with the frontal and temporal lobes were estimated, utilizing multiple linear regression models. Data are presented as the *β*s. Significance was determined through the FDR-corrected *P* value. **B)** The associations of SUHI intensity with MD and ISOVF values of white matter tracts were estimated, utilizing multiple linear regression models. Data are presented as the *β*s. Significance was determined through the FDR-corrected *P* value. **C)** The associations of SUHI intensity with frontal and temporal lobes were stratified by sex. **D)** The associations of SUHI intensity with MD and ISOVF values of white matter tracts were stratified by sex. The *P* for interaction was evaluated using a multiplicative scale, whereby a product term was incorporated into the model to test the statistical significance of heterogeneity. Brain structure with an asterisk indicates the negative association of statistical significance ($P < 0.05$).

air pollution, and wildfires, were suggested to be linked to disease burdens of schizophrenia (Bai et al., 2024; Crank et al., 2023; Liu et al., 2021; Shen et al., 2024; Zhu et al., 2024). The short-term effects of heat waves on schizophrenia hospitalizations have been reported in several cities. A study in China observed higher temperature contributed to a 5.05 % increased risk of schizophrenia hospitalizations, especially in those over 40 years old, men, and non-married (Pan et al., 2019). Similar adverse effects were reported in the US and Canada (Crank et al., 2023; Tupinier Martin et al., 2024). Heat waves might triple the risk of death among individuals with mental illness, and schizophrenia has been identified as a key factor in heat-related deaths (Lee et al., 2023). Our findings enrich

existing epidemiological evidence about the long-term effects of UHI on the onset of schizophrenia, and our observations about brain microstructures may also provide more perspectives for exploring the corresponding mechanism.

Several potential pathways may explain how urban heat exacerbates the risk of SSD onset. Prolonged and intense heat waves may reduce the chance of nighttime cooling, leading to sleep disturbances and deprivation, these factors are directly associated with increased aggression and SSD onset (Obradovich et al., 2017). Meanwhile, long-term exposure to urban heat increases hopelessness, maladaptive anxiety, and stress and may be associated with frequent occurrence of extreme events (Clayton, 2020; Taylor, 2020). Evidence showed that external stressors, such as living in a heated urban environment, can intensify pre-existing mental health conditions, and individuals exhibiting SSD prodromal symptoms or with high genetic risk tend to live in urban regions (Maxwell et al., 2021; Pedersen, 2015). Thus, those with prodromal symptoms may experience cognitive impairment that impairs their ability to cope with heat, potentially leading to a worsening of their mental health condition (Williams et al., 2022). In addition, rising ambient temperatures may elevate the risk of viral infections, which in turn could mediate an indirect biological pathway linking climate change to the onset of schizophrenia spectrum disorders (Liang et al., 2024).

There remains controversy about the vulnerable population of urban heat (Westaway et al., 2015; White, 2024). We found that the UHI effect on SSD was more pronounced among middle-aged adults than older adults. The results are consistent with a US study, which observed increased risks of emergency department visits during extreme heat by 10.3 % in people aged 45–54 years, and 3.6 % in people aged 75 years and older (Sun et al., 2021). It could be explained by the fact that working-age adults are more prone to engaging in occupational and recreational activities that increase their exposure to elevated temperatures, whereas older people spend more time in indoor environments and have lower intensity in outdoor activities (Hansen et al., 2012; Schehl and Leukel, 2020). Moreover, increased heat awareness among older people and several heat stress mitigation interventions might effectively reduce heat-related health risks in the older population (Bassil and Cole, 2010; Seino et al., 2024). We also found individuals with less diligent personality traits were more susceptible. However, evidence about the impact of personality traits on susceptibility to heat stress is rare. We speculated that individuals with less diligent personality traits might lack proactive adaptive behaviors (e.g., taking protective measures), and less mental resilience, resulting in greater stress and discomfort when exposed to high temperatures. Our findings of positive associations of UHI effect with MD and ISOVF values could be explained by the hypothesis that heat-induced damage to the brain endothelial cells of the blood-brain barrier leads to destruction, leakage of serum proteins, evident neuronal axon damage, and the potential development of cerebral edema (White, 2024). Heat stress could also result in the up-regulation of several pro-inflammatory cytokines within the body and central nervous system, such as IL-6 (White, 2024), which was positively related to the volumes, mean thickness, and sizes of specific regions for grey matter in developmental neuropsychiatric disorders, including schizophrenia (Williams et al., 2022). In our study, brain MRI measurements predated the time most participants developed SSD, leading to the results showing increased brain volume and this could be brain edema in pre-schizophrenia (Doron et al., 2021). With the later stages of cerebral edema, brain volumes might gradually atrophy and patients might develop SSD (Jauhar et al., 2022; Zhang et al., 2021).

Mitigating the UHI effect requires coordinated approaches and actions at the global, national, and local levels. Government-mandated policies should give priority to raising climate targets, curbing emissions, building resilience, and advancing science. The United Nations 2030 Agenda for Sustainable Development and the Paris Agreement have been established with the objective of facilitating the creation of a resilient, equitable, and prosperous future for all. It is imperative to make cities an integral part of the solution in fighting climate change (Li et al., 2024). The implementation of adaptation plans, such as climate-sensitive urban design, heat health warning systems, and heat action plans, is important to reduce and prevent the adverse effects of urban heat. In addition, climate models (e.g., microclimate model ENVI-met) could be employed to evaluate proposed UHI mitigation strategies at varying temporal and spatial scales. Furthermore, the efficacy of adaptation strategies may be restricted by socioeconomic and cultural factors. Promoting the understanding of how heat affects diverse populations, with a focus on high-risk communities and more inclusive planning processes, may facilitate equity. A novel concept, climate gentrification, posits that the greening of neighborhoods and the concomitant enhancement of the built environment can frequently result in the displacement of economically disadvantaged communities from their traditional neighborhoods or from areas where they have been residing. Hence, it is essential to ensure that, in the process of implementing these solutions, improvements are made in terms of accessibility and equity so that the most vulnerable individuals continue to have access to these enhanced environments, which will contribute to improved mental health and sustainable development in urban communities worldwide.

The UK Biobank dataset with deep genetic, MRI phenotyping, physical, and healthy data collected from a large sample offered a distinctive opportunity to elucidate the underlying associations between the UHI effect and incidence risk of schizophrenia as well as the interaction with genetic risk. Nevertheless, the project has several limitations. First, the estimate of the UHI effect at residential places could not represent individual exposure precisely due to several extraneous factors (e.g., time spent outside, and others), which could potentially lead to misclassification of exposure. Second, SSD and schizophrenia were identified according to the ICD code without rigorous clinical interviews, possibly leading to misdiagnosis. It was also likely that some participants were undiagnosed, which might lead to the underestimation of the association. However, it is not always feasible to conduct rigorous clinical interviews in large-scale epidemiological studies. The ICD-10 code of schizophrenia has been validated by demonstrating a high level of agreement with the DSM-IV diagnosis (Jakobsen et al., 2005). Third, several unmeasured confounding factors (e.g., physiological vulnerabilities and life stress) could not be ruled out and might weaken the estimates. Fourth, the current study design might lead to potential reverse causation although participants who developed schizophrenia at baseline were excluded. Previous studies observed individuals exhibiting schizophrenia prodromal symptoms or with high genetic risk were inclined to relocate toward urban regions (Maxwell et al., 2021; Pedersen, 2015). Finally, the participants from the UK Biobank were predominantly white, tended to be healthier, and had relatively higher socioeconomic status. Such selection bias might mislead the association and limit the generalizability of the findings.

5. Conclusions

This study showed long-term exposure to UHI could be a latent environmental trigger of new-onset SSD and abnormalities of SSD-related brain microstructures. The population with a high genetic risk of schizophrenia and those aged below 60 years could be more vulnerable and should be prioritized if relevant policies or regulations are developed. The findings may contribute to the establishment of an epidemiological evidence system for both environmental risk determinants of SSD and the long-term effect of UHI on humans, while also offer insights into the development of heat resilience solutions and public health interventions for maintaining thermal comfort for urban residents and controlling the elevating disease burdens of public mental illness. As cities are crucial parts of mitigating climate change, the future of cities and populations should consider joint urban planning and public health frameworks with improved urban climate resilience, enhanced urban sustainability, and advanced public mental well-being.

CRediT authorship contribution statement

Lefei Han: Writing – original draft, Visualization, Methodology. **Yujia Bao:** Writing – original draft, Formal analysis, Data curation. **Jiawei Gu:** Writing – review & editing, Validation. **Yongxuan Li:** Resources, Formal analysis. **Chen Shen:** Software. **Shengzhi Sun:** Writing – review & editing, Supervision, Conceptualization. **Jinjun Ran:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization.

Code availability

Data analysis and results representation were produced by R software (https://www.r-project.org/), ESRI ArcGIS (https://www.esri.com), and BioRender (https://app.biorender.com/). The codes in detail for statistical analysis are available upon request from corresponding authors.

Declaration of competing interest

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.uclim.2025.102435.

Data availability

The data used in the present study are available from the UK Biobank with restrictions applied. Access to the UK Biobank data can be requested through a standard protocol (https://www.ukbiobank.ac.uk/register-apply/). This research has been conducted with UK Biobank Resource under Application Number 99001 (2023-01-31 to 2026-01-31). The data of urban heat island exposure used in this study were provided by the Google Earth Engine, which can be obtained at https://earthengine.google.com/.

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