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Relationship between global warming and autism spectrum disorder from 1990 to 2019

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Background

Despite mounting evidence linking neurological diseases with climate change, the link between autism spectrum disorder (ASD) and global warming has yet to be explored.

Aims

To examine the relationship between the incidence of ASD and global warming from 1990 to 2019 and estimate the trajectory of ASD incidence from 2020 to 2100 globally.

Method

We extracted meteorological data from TerraClimate between 1990 and 2019. To estimate the association between global ASD incidence and temperature variation, we adopted a two-stage analysis strategy using a generalised additive regression model. Additionally, we projected future ASD incidence under four representative shared socioeconomic pathways (SSPs: 126, 245, 370 and 585) by bootstrapping.

Results

Between 1990 and 2019, the global mean incidence of ASD in children under 5 years old was 96.9 per 100 000. The incidence was higher in males (147.5) than in females (46.3). A 1.0 °C increase in the temperature variation was associated with a 3.0% increased risk of ASD incidence. The association was stronger in boys and children living in a low/low-middle sociodemographic index region, as well as in low-latitude areas. According to the SSP585 scenario, by 2100, the children living in regions between 10 and 20° latitude, particularly in Africa, will experience a 68.6% increase in ASD incidence if the association remains. However, the SSP126 scenario is expected to mitigate this increase, with a less than 10% increase in incidence across all latitudes.

Conclusions

Our study highlights the association between climate change and ASD incidence worldwide. Prospective studies are warranted to confirm the association.

Keywords

Autism spectrum disorder; temperature variation; shared socioeconomic pathways.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that affects social interaction, communication and behaviour for life.[1] Based on reports from 11 states in the USA, the prevalence of ASD among 8-year-old children has increased dramatically from 1 in 69 in 2012 to 1 in 36 in 2020.[2,3] This trend has also been observed in countries with high sociodemographic indexes (SDI).[4] The onset of ASD remains elusive, and effective support is yet to be found. Families caring for individuals with ASD face significant challenges.[5] Existing evidence suggests that approximately 50% of clinical ASD diagnoses can be attributed to heritability,[6] indicating that environmental insults and gene-environment interactions also play an important role in the development of ASD.[7,8]

Climate change, particularly global warming, is a critical situation that threatens current and future generations. The global surface temperature was 1.09 °C higher in 2011–2020 than the pre-industrial (1850–1900) level.[9] Without effective action, this trend is predicted to worsen by approximately 0.2 °C per decade. The effects of global warming are diverse and far-reaching, including the spread of vector-borne diseases and rising sea levels.[10] Some studies have examined the relationship between temperature variation and neurological diseases. It is well known that the intensification of heat waves increases the risk of heat stroke.[11] High temperatures have been associated with an increased incidence of neurodegenerative diseases such as Alzheimer's dementia, epilepsy and Parkinson's disease.[12] There is limited research on the impact of high temperatures on neurodevelopmental disorders, which develop predominantly during childhood.

We investigated the association between global warming and ASD incidence globally using data derived from 204 countries and territories over 30 years.[13] Furthermore, we projected future changes in ASD incidence under four shared socioeconomic pathways (SSPs: 126, 245, 370 and 585).[14] Our hypothesis was that elevated temperature variation would be positively associated with an increased risk of ASD incidence.

Method

GBD data

The Global Burden of Disease (GBD) Results Database is publicly available. It contains data on the prevalence, incidence, and disability adjusted life years (DALYs) of 369 diseases and injuries worldwide from 1990 to 2019.[15] In GBD 2019, children with ASD were diagnosed using the Diagnostic and Statistical Manual of Mental Disorders (DSM: III, III-R, IV, IV-TR, 5), the International Classification of Diseases (ICD: 9, 10) and the Chinese Classification of Mental Disorders (CCMD). Data on the incidence of ASD in children under 5 were extracted from the database, as ASD is more commonly identified in this age group.

The Sociodemographic Index (SDI) is a comprehensive index for evaluating a country's level of development. It takes into account the average years of schooling and per capita income of females over 15, as well as the fertility rate of females under 25.[16] Additionally, GBD provides data on $PM_{2.5}$, a risk factor for neurological disorders, for the years 1990, 1995, 2000 and 2005 and from

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2010 to 2019. We estimated unavailable data by the mean value closest to the available data. For example, the concentration of $PM_{2.5}$ in 1991 was estimated as the mean value of 1990 and 1995. The $PM_{2.5}$ data were categorised into quartiles (5–15 μg/m^3; 15–27; 27–35; >35).[15] Unlike epidemic diseases, which were categorised into 21 geographical regions in most GBD studies, we grouped the 204 countries/locations by latitude to study non-communicable diseases. To better understand the influence of climate, we categorised all countries/locations by 10° of their mean latitude. We also combined countries/locations with latitude above 50° for statistical power. More information can be found in Supplementary Table 1 available at https://doi.org/10.1192/bjo.2024.790.

Climate data

TerraClimate is a global database that provides monthly meteorological and water balance variables with a resolution of 4 km. It spans over 60 years and includes a range of climate variables, such as maximum and minimum temperatures, precipitation, wind speed, soil moisture and vapour pressure deficit.[17] These climatic variables were extracted based on shapefiles of the first-level administrative areas of GBD countries/locations. To account for seasonal and geographical differences, we calculated the maximum temperature of a year by averaging the highest four monthly temperatures. Moreover, we averaged 12 months of soil moisture, precipitation and wind speed measurements to represent their annual values.

In our study, we employed the yearly change of high temperatures to investigate the impact of global warming. To determine the variation, we first identified the 'ideal' temperature by selecting the lowest maximum temperatures from 1990 to 2019, using the year with the lowest temperature as the reference year. The maximum temperature variation was then defined as the difference between the maximum temperature of a given year and the 'ideal' temperature, reflecting heat-related changes over 30 years.

Prediction data

The Coupled Model Intercomparison Project Phase 6 (CMIP6) data-set provides climate data for past, present and future periods.[14] Ten general circulation models (ACCESS-ESM1-5, CanESM5, CESM2, FGOALS-g3, GFDL-ESM4, HadGEM3-GC31-LL, IPSL-CM6A-LR, MIROC6, MRI-ESM2-0 and NorESM2-LM) were considered in the study. To collect this data on a global scale, we utilised a 20 km × 20 km fishnet to identify 474 975 locations within all GBD countries and territories. To achieve full coverage, we added 11 additional locations (Niue, Cook Islands, Bermuda, Marshall Islands, Monaco, Nauru, Maldives, San Marino, Tuvalu, Tokelau, American Samoa) that were not previously captured by the fishnet. We extracted the monthly high temperature values in these locations under four SSPs. We calculated new maximum temperature variations based on these models, and then averaged them at 20-year intervals, covering the periods 2021–2040, 2041–2060, 2061–2080 and 2081–2100, respectively.

Statistical method

We utilised a two-stage analysis to carry out an ecological trend study in which we investigated the association between the maximum temperature variation and the incidence of ASD. In the first stage, we employed a generalised additive regression model to explore the associations between ASD incidence and each climate variable. The variables with significant differences were selected for further analysis, and the maximum temperature variation was found to be the most potent.

In the second stage, we used a generalised additive regression model to explore the association between ASD incidence and temperature variation. We employed a forward stepwise selection method, using the likelihood-ratio test to compare models, and incorporated each variable that showed a significant difference. In the fully adjusted model, we included demographic, socioeconomic, geographic and environmental covariates, such as gender, SDI, $PM_{2.5}$, latitude, wind speed and mortality of children under 5. Additionally, subgroup analyses were conducted based on gender, latitude and SDI. To fill the gap in $PM_{2.5}$ data in previous years, we used 10-year integral data from 2010 to 2019 with the final model for sensitivity analyses.

All associations were presented as odds ratios with corresponding 95% confidence intervals. In this study, the odds ratios represent the change in ASD incidence for every 1 °C increase in maximum temperature variability. A two-sided *P*-value <0.05 was considered statistically significant. The statistical analyses were performed using R Studio Version 1.2.5042 for Windows (The R Project for Statistical Computing, Vienna, Austria).

For the prediction step, we assumed that the relationship between maximum temperature variation and the incidence of ASD would remain constant in the future, with minimal changes to socioeconomic factors. We extracted future CMIP6 meteorological data and calculated new maximum temperature variation. We conducted one projection with 10 000 randomly selected points from different latitude groups (0–10°: 43 125 points, 10–20°: 59 590, 20–30°: 72 593, 30–40°: 61 583, 40–50°: 61 250, >50°: 176 834). We conducted 10 000 simulations and then visualised these changes under four SSPs: 126, 245, 370 and 585).

Results

From 1990 to 2019, the global average incidence of ASD in children under 5 was 96.9 per 100 000 population (Table 1). Boys were more likely to be affected than girls, with a ratio of over 3:1. The incidence of ASD followed a 'U' shape in relation to factors such as SDI, latitude and $PM_{2.5}$. The global mean maximum temperature was 29.4 °C (Supplementary Table 2). The regions between 0 and 20°

Table 1 The distribution of autism spectrum disorder incidence from 1990 to 2019

	Incidence	*P* value
Global	96.9 (57.2)	
Gender		<0.001
Male	147.5 (36.5)	
Female	46.3 (9.7)	
SDI		<0.001
Low	100.9 (50.3)	
Low-middle	86.4 (45.6)	
Middle	87.4 (50.0)	
High-middle	98.2 (64.0)	
High	122.8 (82.5)	
Latitude (°)		<0.001
0–10	97.5 (52.3)	
10–20	90.0 (47.6)	
20–30	83.3 (44.5)	
30–40	102.4 (64.6)	
40–50	102.2 (63.6)	
>50	119.9 (78.3)	
$PM_{2.5}$ (μg/m^3)		<0.001
5–15	102.5 (69.6)	
15–27	96.6 (58.0)	
27–35	92.8 (49.4)	
>35	95.8 (49.1)	

SDI, sociodemographic index; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5 μm. The incidence with s.d. was calculated as new cases per 100k population. $PM_{2.5}$ was categorised in terms of quartiles.

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Table 2 The association between autism spectrum disorder incidence and temperature variation from 1999 to 2019

	OR (95% CI)		
	Model 1	Model 2	Model 3
Global	1.06 (1.03, 1.07)	1.04 (1.03, 1.05)	1.03 (1.02, 1.04)
Latitude (°)			
0–10	1.16 (1.14, 1.18)	1.08 (1.06, 1.10)	1.08 (1.06, 1.09)
10–20	1.12 (1.11, 1.14)	1.08 (1.07, 1.10)	1.08 (1.07, 1.10)
20–30	1.12 (1.10, 1.14)	1.08 (1.07, 1.10)	1.07 (1.05, 1.09)
30–40	1.08 (1.06, 1.09)	1.07 (1.05, 1.08)	1.06 (1.04, 1.07)
40–50	1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.05 (1.04, 1.06)
>50	1.00 (0.99, 1.02)	1.00 (0.99, 1.01)	0.99 (0.98, 1.00)

Model 1 was adjusted for gender, SDI, $PM_{2.5}$, year and latitude. Model 2 further adjusted for climate factors (soil moisture, precipitation and wind speed). Model 3 further adjusted for the mortality of children under 5 years. All results were represented with ORs and a 95% CI.
OR, odds ratio; SDI, sociodemographic index; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5 μm.

latitudes had higher average soil moisture and precipitation compared with other areas. Conversely, wind speed showed the opposite pattern. The levels of $PM_{2.5}$ were higher in areas located between 10 and 20° latitudes. The global mean maximum temperature variation was 1.19 °C. The variation increased with the increase of SDI and latitude. The majority of reference years were in the 1990s, such as 1992, 1993 and 1996 (Supplementary Table 3).

In the preliminary analysis, all climatic factors were associated with ASD incidence (Supplementary Table 4). After full adjustments, an increase of 1.0 °C in maximum temperature variation was positively associated with a 3% increased risk of ASD incidence (95% CI: 1.02–1.04). The association was stronger for children living in low-latitude regions, which was also found in sensitivity analyses (Table 2, Supplementary Table 5). In subgroup analysis, we found that the relationship was more pronounced in male children (odds ratio, 1.04; 95% CI: 1.03–1.05), as well as in those living in low or low-middle SDI countries (odds ratio, 1.12; 95% CI: 1.11–1.14; odds ratio, 1.16; 95% CI: 1.14–1.17, respectively), and those in the lowest quartile of $PM_{2.5}$ (odds ratio, 1.03; 95% CI: 1.02–1.04), as shown in Table 3.

Figure 1 shows that the slopes of the increase in ASD incidence are in ascending order from mild to severe greenhouse gas emissions except for locations at above 50° latitude. Between 2020 and 2100, the mean temperature increase under SSP585 varies from 4.6 °C to 10.1 °C at elevated latitudes, while the changes under SSP126 range from 0.2 to 0.6 °C. The incidence of ASD remains stable from 2040 to 2100 at all latitudes under SSP126, which implies the adoption of sustainable, low-carbon lifestyles aimed at mitigating global warming (Figs. 1(a)–1(e), 1.18% per 20 years, 1.74%, 1.42%, 1.40%, 1.49%). In contrast, the SSP585 scenario, which lacks control of climate change, leads to a substantial surge in ASD incidence by 45.8%, 68.6%, 48.6, 51.4 and 40.8% in Figs. 1(a)–1(e) as of 2100, respectively. We observed moderate increases in ASD incidence under SSP245 and SSP370, which are intermediate pathways with balanced development trends in all dimensions.

Table 3 Subgroup analysis between covariates and temperature variation

	OR (95% CI)	*P* value
Gender		<0.001
Male	1.04 (1.03, 1.05)	
Female	1.01 (1.00, 1.02)	
SDI		<0.001
Low	1.12 (1.11, 1.14)	
Low-middle	1.16 (1.14, 1.17)	
Middle	1.10 (1.09, 1.11)	
High-middle	1.05 (1.04, 1.06)	
High	0.99 (0.98, 1.00)	
$PM_{2.5}$ (μg/m^3)		<0.001
5–15	1.03 (1.02, 1.04)	
15–27	0.98 (0.97, 0.98)	
27–35	0.99 (0.99, 1.00)	
>35	0.95 (0.95, 0.96)	

OR, odds ratio; SDI, sociodemographic index; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 μm. All results were represented with ORs and 95% CI.

Discussion

This study is the first of its kind to assess and quantify the global risk of ASD associated with climate change-related temperature variation, and then simulate future incidence of ASD by bootstrapping. Our findings suggest that ASD incidence is associated with maximum temperature variation, which reflects the frequency and severity of temperature spikes resulting from global warming. Additionally, our results indicate that the association is more pronounced among boys and children living in areas with a low/low-middle SDI and in low-latitude regions.

According to the GBD Study 2019 report, neonatal disorders remained the leading cause of DALYs for children under 10 years old from 1990 to 2019.[15] The age-standardised rate increased from 9.17 per 100 000 to 9.32 during that period.[4] The impact of climate change on mothers and infants is extensive and profound, which is consistent with the risk factors of ASD and the morphologic and molecular changes in ASD children and ASD animal models.

We summarised potential pathways between global warming and ASD in Fig. 2. High temperatures are associated with psychological health conditions, including depression and anger.[18] They can lead to epigenetic changes in mothers that may be inherited by their offspring,[19] and can reduce cerebral blood supply by affecting maternal epinephrine levels, potentially increasing the risk of adverse birth outcomes.[20] Moreover, global warming has a significant impact on food access that can have consequences for maternal nutritional deficiencies,[21] directly affecting fetal development due to insufficient folic acid intake and infant development due to inadequate feeding practices.[22] Mothers who experience malnutrition during pregnancy are more susceptible to infections, and the use of acetaminophen has been identified as an independent risk factor for ASD.[23] Temperature changes are closely associated with the spread of pathogenic microorganisms, posing a greater risk to infants with weakened immune systems.[24] Infection-induced immune activation alters cytokine levels in the blood, potentially leading to reactive glia.[25] The interaction between microglia and astrocytes not only triggers neuroinflammation but also disrupts the blood–brain barrier (BBB), exacerbating central nervous system (CNS) inflammation as immune cells like TNF-α and IL-6 migrate to the brain through the BBB with increased permeability.[26] Animal studies have found that heat can directly damage the BBB, especially in young rats.[27] These changes may modify synaptic morphology, including reduced dendritic branching and increased spine density, disrupt the brain homoeostasis of inhibitory and excitatory transmission contributing to abnormal synaptic plasticity, and atypical connectivity of specific brain regions.[28,29] Immune dysfunction and synaptic deficits have also been observed in mouse models of ASD.[30] Structural alterations in the hippocampus, that is an important region for social and cognitive function in ASD children, have been widely documented.[31] Hyperthermia can cause febrile seizure by suppressing gamma-aminobutyric acid (GABA)-ergic synaptic transmission in CA1 neurons, particularly in immature animals.[32] Febrile seizure during infancy may underlie the development of temporal-lobe epilepsy, a common comorbidity in children with ASD.[33,34] In addition, high temperatures can affect

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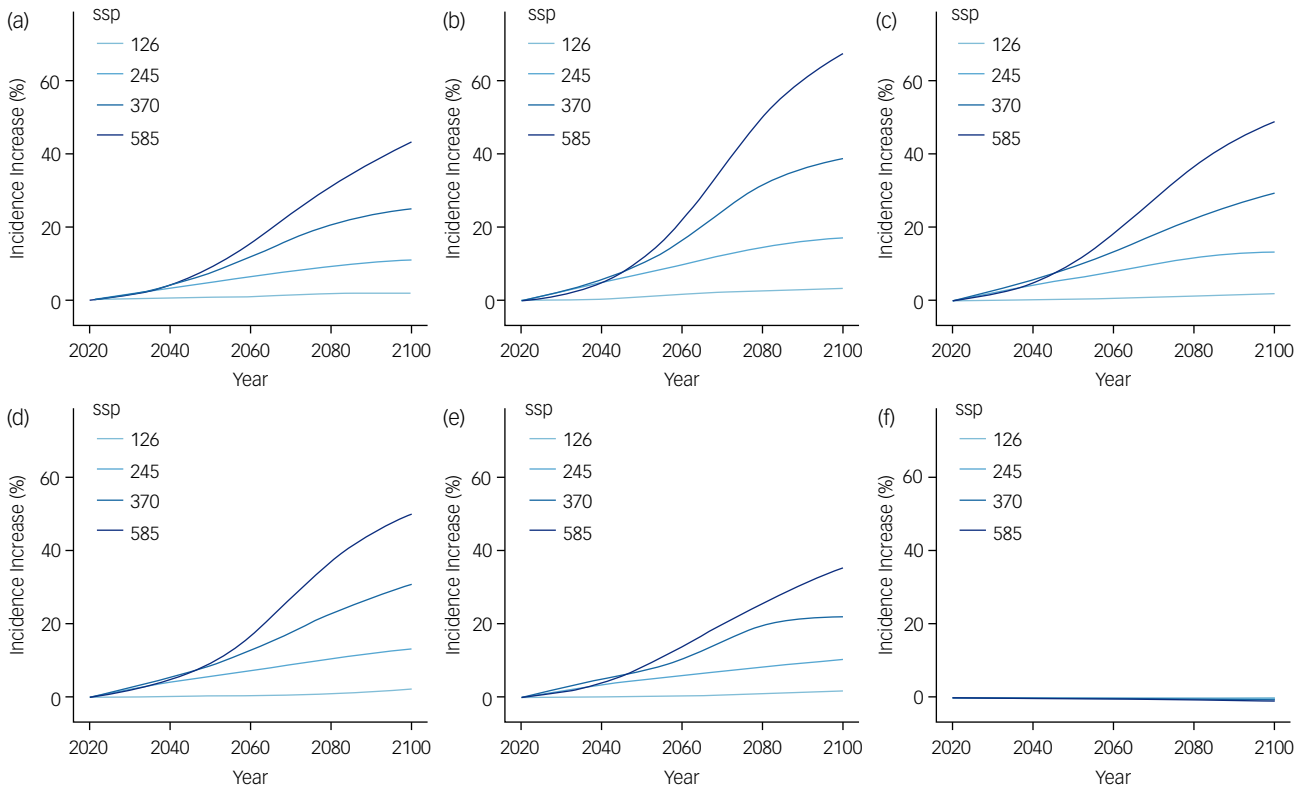

Fig. 1 The projection of autism spectrum disorder incidence increase as of 2100 under SSP126, SSP245, SSP370 and SSP 585. Figure 1 represent changes in future ASD incidence away from the equator respectively: (a) the projection at 0–10° latitude; (b) the projection at 10–20° latitude; (c) the projection at 20–30° latitude; (d) the projection at 30–40° latitude; (e) the projection at 40–50° latitude; (f) the projection at above 50° latitude. SSP, socioeconomic pathway.

sleep in both mothers and infants, impacting synaptic plasticity.[35] Global warming can worsen air pollution through increased wildfires, which has been associated with maternal and birth complications that are related to ASD development.[36] Moreover, black carbon has been detected in the cord blood and fetus brains, and the particles can induce neuroinflammation.[37]

Countries with high SDI usually have a low $PM_{2.5}$ concentrations. They may benefit from improved screening and diagnostic

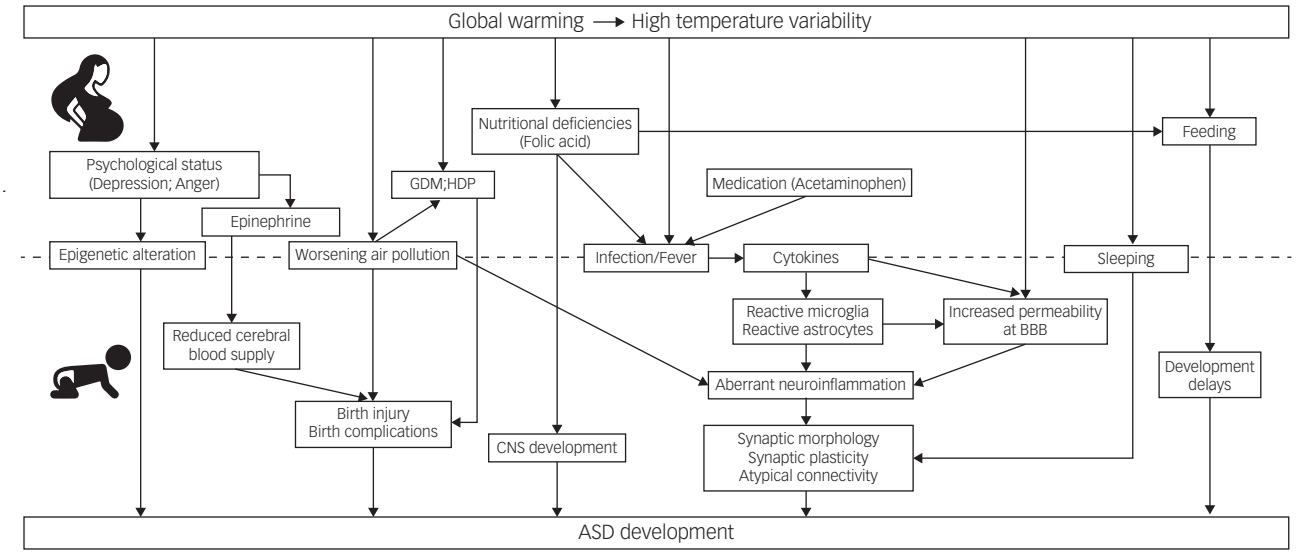

Fig. 2 Potential pathways between global warming and ASD. The boxes above the dashed line represent factors that may affect mothers. The boxes on the dashed line may impact both mothers and offspring. The boxes below the dashed line represent factors that may affect offspring. ASD, autism spectrum disorder; GDM, gestational diabetes mellitus; HDP, hypertensive disorders of pregnancy; CNS, central nervous system; BBB, blood–brain barrier.

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capacity, as well as the availability of disability living allowances, which could potentially increase the detection of ASD.[38]

If the association remains, according to the projections, high levels of emissions will lead to an increase in ASD incidence worldwide. Children living in regions between 10 and 20° latitude are at a higher risk of being affected. Certain African countries, including Angola, Chad, Malawi, Mali, Sudan, Senegal and Zimbabwe at this latitude, are expected to experience severe warming. Moreover, the incidence of ASD has increased in North Africa and the Middle East from 1990 to 2019.[39] This is unjust as lower-income countries with low carbon emissions in low-latitude areas are disproportionately affected by climate change, whereas high-income countries located above 50° latitude generate high carbon footprints but are hardly affected.[40]

Our research has some limitations. The absence of standard diagnostic criteria in all GBD countries and territories may underestimate the incidence of ASD in developing and underdeveloped regions, and improved awareness of ASD and changes in diagnostic criteria of ASD are not taken into account in the study. Additionally, GBD data are imputed based on a standardised Bayesian regression tool, which introduces some uncertainty in the estimates. There is usually a time lag between the development of ASD and exposure to temperature perturbations, which we could not address because of the lack of fine temporal epidemiological data. It is important to note that the absence of data in Africa can lead to assumptions being made using data from neighbouring countries, which can further widen the confidence interval. Furthermore, using a single value to represent incidence, latitude and meteorological indices may weaken the association between temperature variation and ASD incidence in several large countries. As this is an ecological trend study, individual data are not available, and a causal relationship cannot be demonstrated. Thus, the results should be interpreted carefully.

At the Sixty-Seventh World Health Assembly in 2014, a resolution was passed with the aim of optimising the development, health, well-being and quality of life of individuals with ASD through comprehensive and coordinated efforts. Our study, from a global standpoint, has shown that climate change is associated with ASD incidence. However, further prospective studies are warranted to confirm the association. If high temperatures are indeed a risk factor for the development of ASD, it is crucial to reduce exposure to extreme heat and take measures to mitigate climate change. This is especially important in countries with lower incomes, to alleviate their healthcare burdens. These actions will ultimately improve children's well-being and support the goals outlined in the WHO's Comprehensive Mental Health Action Plan 2013–2030.

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Supplementary material

Supplementary material is available online at https://doi.org/10.1192/bjo.2024.790

Data availability

The data for this study (Global Burden of Disease (GBD) data-set, TerraClimate data-set, Coupled Model Intercomparison Project Phase 6 (CMIP6) data-set) are publicly available. The GBD data-set can be accessed at https://vizhub.healthdata.org/gbd-results/; the TerraClimate data-set can be accessed at https://climate.northwestknowledge.net/TERRACLIMATE/; and the CMIP6 data-set can be accessed at https://wcrp-cmip.org/cmip6/.

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Author contributions

Q.Z.: conceptualisation, methodology, formal analysis, writing original draft, review and editing. J.C.: conceptualisation, methodology, formal analysis. J.M., R.D., W.J., Z.L.: data collection, review and editing. L.L., Q.Q., S.S., Y.J., Y.P., Z.Z.: supervision.

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Declaration of interest

The authors declare that they have no conflict of interest.

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