Imperatives and co-benefits of research into climate change and neurological disease [Au: title change OK?] ok

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Abstract | Evidence suggests that anthropogenic climate change is accelerating and is affecting human health globally. Despite urgent calls to address health effects in the context of the additional challenges of environmental degradation, biodiversity loss and ageing populations, the effects of climate change on specific health conditions are still poorly understood. Neurological diseases contribute substantially to the global burden of disease, and the possible direct and indirect consequences of climate change for people with these conditions are a cause for concern. Unaccustomed temperature extremes can impair the brain's systems of resilience, thereby exacerbating or increasing susceptibility to neurological disease. In this Perspective, we explore how changing weather patterns resulting from climate change affect sleep — an essential restorative human brain activity, the quality of which is important for people with neurological diseases. We also consider the pervasive and complex influences of climate change on two common neurological conditions: stroke and epilepsy. We highlight the urgent need for research into the mechanisms underlying the effects of climate change on the brain in health and disease. We also discuss how neurologists can respond constructively to the climate crisis by raising awareness and promoting mitigation measures and research, actions which will bring widespread co-benefits. **[Au: changes to the Abstract OK, to conform to the 200-word limit for this section?] ok – I would like to bring 'co-benefit' back – addition ok?**

[H1] Introduction **[Au: I have added the markers [H1], [H2] and [H3] to keep track of the different subheading levels during editing — the markers will be removed before publication]ok**

Anthropogenic climate change is profoundly affecting every part of the planet. The 1.5°C limit on global warming **[Au: OK?] not sure 'limit' has the right meaning here – was really only an 'aspirational threshold'** set by the 2015 United Nations Framework Convention on Climate Change Paris Agreement was first breached over a 12-month period between 2023 and 2024, increasing the risks of global adverse climate effects even sooner than predicted. We are far from understanding the complex outcomes of these dramatic changes (Box 1), but authoritative studies, such as the Lancet Countdown reports, indicate that climate change is already substantially harming **[Au: OK, to streamline the text? Also, please note that our preference is to use 'significantly' only when referring to statistical significance]** ok human health and the natural world[1,2]. Climate change is associated with increased death rates, especially with heatwaves across climate zones[3-8], and heat-related mortality is projected to rise further in the coming years **[Au: OK?]ok**[9,10]. **[Au: I have moved the reference to Box 2 to the end of this section]ok**

The health consequences of climate change are expected to be particularly severe for very young, elderly and other vulnerable populations[11,12] **[Au: changes to this sentence OK?]ok**. The 'vulnerable' category is diverse and includes pregnant women, outdoor workers and people who sleep rough, are new to an environment, or have chronic diseases and/or **[Au: OK? Many people with chronic diseases will be on medications]ok** are on medications. People with neurological diseases are rarely considered despite the fact that these conditions contribute substantially to global disability-adjusted life years (DALYs) and mortality **[Au: changes to this sentence OK?]ok**. One in six people have a neurological condition, and such conditions featured prominently among the causes of death from the 2003 heatwave in France[13] and the 2022 heatwave in the UK[14]. **[Au: changes OK? I couldn't find the figures that you quoted in the cited articles (for example, of 15,000 excess deaths during the French heatwave, only 1,001 were attributed to neurological causes, so it's not clear where the one-quarter figure came from)]ok – I calculated this taking into account all deaths with neurological involvement, but ok with your edit** Although 'brain health' is considered to be pivotal to all 17 of the United Nations Sustainable Development Goals[15], and the possible impact of climate change on neurological health has been acknowledged[17,18], the new WHO Intersectoral Global Action Plan on epilepsy and other neurological disorders (2022–2031), which aims to improve quality life of people with neurological disorders, does not mention climate change[16]. People with neurological diseases typically have impaired resilience to environmental challenges[19-22], and these individuals, along with their families and carers, are understandably concerned about the prospect of climate change[17]. **[Au: changes to the last part of this paragraph OK? The original ordering of the text seemed a little disjointed]ok. Does 'prospect' suggest a future thing rather than a now thing?**

In this Perspective, we explore the complexity of the interactions between the effects of climate change, such as extreme temperatures, altered weather patterns and increased air pollution, **[Au: OK to provide specific examples of the effects of climate change?]ok** and the brain in both health and disease. Rather than attempting to cover the full spectrum of neurological diseases, some of which have been reviewed in relation to climate change elsewhere[17,23,24], we focus on three main areas **[Au: changes to this sentence OK, to streamline the text?]**.ok First, we consider sleep, because it is an essential component of human and brain health, and many neurological conditions are aggravated when sleep is compromised[25,26]. Second, we consider stroke, as it contributes substantially to the global burden of disease, and much research on its relationship with **[Au: changes OK?]ok** climate change has been published. Last, we consider epilepsy as another globally burdensome condition that is a focus for the WHO 2023 Intersectoral Global Action Plan[16]. To aid comprehension of the subject area, Box 2 provides definitions of terms that are commonly used in relation to climate change. **[Au: OK?]ok**

[H1] Temperature and the nervous system

[H2] Effects on neurons

All cellular proteins have intrinsic temperature dependence, which is determined by the protein structure and is expressed as the temperature coefficient Q_{10} — the change in function that occurs in response to a 10°C change in ambient temperature. Ion channels and receptors in the nervous system commonly have Q_{10} values in the 1.5–4.0 range. Animals living in environments with wide (for example, >20°C) ambient temperature ranges, which can also fluctuate from year to year, have evolved to maintain system function in the face of these temperature variations **[Au: changes to this sentence OK?]**[27].ok If the temperature surpasses these boundaries, circuit behaviour is compromised (Figure 1 **[Au: I have edited down the original box text to reduce repetition (see below), and I think this item works better as a figure now]**); different animals with normal robust control behaviour 'crash' with different dynamics[27,28].

Genetic variations in ion channels or other molecules can, in complicated and unpredictable ways, influence how a network will respond to elevated temperature. Networks close to or already experiencing dysfunction for other reasons could be more susceptible to temperature-induced crashes, potentially explaining why individuals with epilepsies or other neurological disorders are particularly sensitive to temperature change.

[H2] Effects on the thermoregulatory system **[Au: please provide references for all of the statements made in this section]suggestions made**

The ‘thermoneutral’ air temperature range in which a resting naked human can thermoregulate without sweating or shivering, by just changing cutaneous blood flow (heat delivery), is 26–28°C. ref: Michael J. Tipton, ... Frank St. C. Golden, in Bove and Davis' Diving Medicine (Fourth Edition), 2004. Chapter 13, Hypothermia.

Heat loss at the skin–environment interface is modified by several factors, including clothing, air movement, water vapour pressure and non-thermal factors, such as medical conditions, certain medications (for example, antidepressants, antipsychotics, some antiseizure medications, antihistamines and anticholinergics), the gut biome, the psychological state and the degree of acclimatization **[Au: changes to this sentence OK? I didn’t think that we needed to name the individual drugs] ok -but then need ‘some’ as no evidence they all do it**. Heat illnesses become increasingly severe, culminating in heat stroke, as the deep body temperature increases from normal (37°C) to lethal levels (>41°C). ref: https://pubmed.ncbi.nlm.nih.gov/30990296/

Human thermoregulation attempts to balance heat gain from metabolism and the environment with heat loss (through skin blood flow and sweating), thereby maintaining a constant **[Au: OK?] – well it is not constant, but varies within a narrow range (even for the brain) – may be ‘narrow internal temperature range’?** internal temperature. This system can place demands on all other bodily systems, including the nervous system.

Cutaneous thermoreceptors transduce temperature into afferent neural discharges, which are integrated in the hypothalamus. Thermosensitive neurons are found in the anterior, preoptic, posterior, lateral, and dorsal hypothalamic areas. Up to 70% of temperature-sensitive hypothalamic neurons are affected by changes in skin or spinal temperature, and around 30% of preoptic neurons are intrinsically responsive to warming. Autonomic thermoregulatory responses (vasoconstriction, vasodilation, sweating and shivering) and behavioural thermoregulatory responses can be evoked by both peripheral and central temperature changes. Responses differ for each stimulus type and could have different roles in mediating neurological responses in both health and disease.

Individual responses and resilience to heat vary considerably and are determined by both genotypic and phenotypic factors **[Au: changes OK?]ok**. Acclimatization to heat over a couple of weeks increases sweat production (with reduced salt content) and expands plasma volume; these changes improve the capacity of the thermoregulatory system to control body temperature at rest, reduce body temperature elevations **[Au: is this what you meant?]** yes during exercise in the heat and increase thermal comfort, thereby reducing psychological stress. The effects of neurological disease on these countermeasures to heat have not been extensively studied to date.

[H1] Climate change and neurological disease

Environmental neuroscience is a discipline that examines brain changes during prenatal development and post-natal life resulting from variations in the physical environment, including exposure to pollutants and differences in socioeconomic status **[Au: changes OK? I wasn't sure what you meant by 'socioeconomic inputs']ok**. To the list of environmental variables, we must now add acute and longer-term exposures to increased and extreme ambient temperatures (heatwaves and cold snaps) and extreme weather events for example, floods and droughts), resulting from climate change and pollution. **[Au: deletion OK? This text seemed misplaced, and you mention the lack of research on the effects of climate change on people with neurological diseases below]ok**

The nervous system has a central role in the detection of and response to environmental changes, including temperature, humidity and pollution, and brain diseases are expected to compromise autonomic and behavioural responses to environmental challenges, including those resulting from climate change **[Au: changes to this sentence OK?]**.ok At the individual level, the effects of disease are compounded by a complex nexus of socioeconomic status, built environment, access to services, local geography, and climate mitigations and adaptations. The role of indoor environmental variables, which might be modified by climate change mitigations such as building fabric energy retrofit, has not been studied extensively to date[29]. However, evidence is mounting that thermally inadequate housing stock magnifies the adverse effects of climate change-related weather and pollution events[30]. Such stock is often situated in already highly polluted, socioeconomically deprived urban areas, thereby amplifying adverse health effects and inequalities. Poor building quality could increase existing localized risks of developing epilepsy and adverse neurodevelopmental outcomes associated with poverty[31-33] **[Au: changes to this sentence OK? The original wording was quite difficult to follow]**.ok

The joint effects of disease and climate change on the health and well-being of people with neurological diseases, and the individual psychology around climate change, including climate anxiety, have not been well studied[34]. Many neurological diseases are associated with increased rates of neurodiversity and psychiatric morbidity, both of which could aggravate the impact of climate change and further impair essential coping responses.

Systems neuroscience approaches, which seek to understand both disease biology and environmental influences in the setting of a changing climate, could generate actions that facilitate climate change mitigation and improve disease prognosis[35]. The neurology field could also learn from people with conditions such as ectodermal dysplasias, who have already developed strategies for coping with heat stress, irrespective of climate change[36].

[Au: changes to this paragraph OK? It was quite 'wordy' in places]yes,a failing of mine. All ok

[H2] Sleep

Sleep is a major determinant of quality of life[37-39]. The sleep–wake cycle is closely linked to environmental cycles through circadian rhythms driven by the hypothalamic suprachiasmatic nucleus. This **[Au: OK?]** endogenous circadian pacemaker is entrained by environmental cues, primarily the light–dark cycle and the associated ambient temperature cycle. Sleep initiation and maintenance are intimately linked to thermoregulation, which is itself affected by many neurological disorders[40,41]. The temperature of the human brain has a pronounced diurnal rhythm[42], the robustness of which predicts survival after traumatic brain injury[43], possibly related to associations between brain temperature and sleep **[Au: changes to this sentence OK?]**.ok

Sleep-wake behaviour is influenced by environmental temperature: exceptionally low and high temperatures disrupt sleep, with extreme temperature events being associated with reduced sleep duration and increased sleep disturbance[44-46] **[Au: deletion OK? The term 'situational insomnia' is not used anywhere else in the article, so the reason for introducing it here was unclear]**. Ok – was used by Derk-Jan to try to make this section more nuanced, but ok In many parts of the world, the rise in environmental temperature attributed to climate change is has been more pronounced at night than during daylight hours[47], which is likely to affect night-time behaviours such as sleep in humans[48] **[Au: changes to this sentence OK?]**.ok **[Au: deletion OK? The previous sentence already alludes to regional variations in night-time temperature changes]ok** One study predicted that a 1°C night-time temperature anomaly would produce almost 9 million additional nights of insufficient sleep per month or 110 million extra nights of insufficient sleep per year across the USA[49]. Older people and other vulnerable groups (including, for example, individuals with sleep apnoea[50,51]), especially those living in deprived areas, are likely to be most affected, thereby amplifying existing social determinants of ill health.

Many neurological diseases disrupt sleep and potentially aggravate sleep problems during heatwaves. In turn, sleep disturbance caused by the effects of climate change could aggravate neurological disease. For example, a bidirectional relationship exists between sleep disturbance and neurodegenerative diseases such as Alzheimer disease and Parkinson disease[52,53,59]. In addition, sleep architecture changes with age: in aged mice, acute sleep deprivation did not appropriately activate the unfolded protein response signalling pathway in the endoplasmic reticulum, thereby increasing the risk of pathogenic protein aggregation[54] **[Au: changes to this sentence OK?]**. ok

Evidence suggests that sleep changes the function of the glymphatic system, which promotes clearance of potentially toxic protein products such as -amyloid-β (Aβ) from the brain. Most research to date indicates that the glymphatic system is most active during sleep[55,56], although one recent study indicated that clearance of proteins from the brain was reduced during sleep[57]. In support of a link between sleep disruption and glymphatic system dysfunction, **[Au: additional text OK?]** poor sleep quality and duration have been shown to correlate with increased Aβ load in the brain[58]. **[Au: deletion OK? The relevance of this**

sentence to glymphatic system dysfunction was unclear. I have moved the ref. 59 citation to the sentence earlier in the paragraph where Parkinson disease is mentioned] ok

Sleep is an important factor in many other neurological diseases[60] and also contributes to the preservation of mental health, which is often impaired in people with neurological disorders[61]. The direct and indirect effects of climate change on sleep and circadian rhythmicity are likely to have serious implications for physical and mental health, brain function, and disease susceptibility and aggravation. Exploring these complex relationships will be crucial to bolster resilience to climate change and, as a co-benefit, to help minimize the risk of developing neurological conditions associated with poor sleep and circadian disturbance. **[Au: changes to this paragraph OK, to streamline the text? The original wording was quite difficult to follow]ok. We had wanted to make the point that sleep disruption from climate change will also affect families and carers with consequences for the care of their charges with neurological diseases.**

[H2] Stroke

[H3] Epidemiology. Cardiovascular disease is the leading cause of death globally, and links to climate change are emerging[62,63]. Stroke shares many risk factors with cardiovascular disease and is the second leading cause of death **[Au: please could you double check this statistic? I can't find it anywhere in ref. 64]** and a major cause of disability worldwide[64]. Between 1990 and 2019, the absolute number of incident stroke cases increased by 70% globally, with 43% more deaths from stroke and 143% more DALYs[65]. The Global Burden of Disease Study 2019 included 'high and low non-optimal' temperatures as a leading risk factor for all-cause mortality **[Au: are you referring to stroke-related mortality or mortality from all causes?]**[64].

The relationship between adverse weather events, temperature extremes, pollution and stroke incidence is complex. Unseasonally hot or cold temperature extremes, unaccustomed diurnal temperature variation and increased pollution levels are all associated with increased stroke incidence, hospital **[Au: OK?]ok** admission and mortality risk, with differing effects by stroke type[17,23]. Rapid temperature falls (cold snaps) are also linked to stroke incidence[23] and mortality[23]. In 2023, a study across 27 countries demonstrated that extremes of temperature were associated with an increased risk of death from any cardiovascular cause[66]: for every 1,000 stroke deaths of 9.3 million studied, 1.6 and 9.0 excess deaths were associated with extreme hot and cold days, respectively. In this study, extreme hot and cold days were defined in comparison to the local average temperature (>97.5th or <2.5th percentiles), accounting for individual adaptation to high or low temperatures at one location, loss of which might be an added risk factor for individuals who migrate or travel.

Gross domestic product (GDP) per capita has been linked to temperature-related stroke deaths, with people living in countries with lower GDP at increased risk of mortality **[Au: please cite the source of this observation — is it still ref. 66?]**.sorry, no - ref 63 The authors suggest that greater ability to control temperature exposures and less unavoidable outdoor work in higher-income countries could contribute to this effect. Of note, data from 2019 showed that 86% of deaths and 89% of DALYs attributable to stroke were in lower-income to upper-middle-income countries[67]. A global population-based study of 204 countries and territories between 1990 and 2019 showed an increasing burden of stroke, partly owing to ageing populations, but also related to non-optimal temperatures — mainly cold temperatures, although higher temperatures seemed to have an increasing role over time **[Au: OK?]**[68]. Ok Discrepancies between low-income and higher-income income countries potentially highlight a means by which excess deaths might be prevented through better access to education, health-care or wider protection from temperature extremes, but more research is required to fully understand the complex underlying mechanisms.

[H3] Mechanisms. Temperature extremes could interact in a number of ways with the cardiovascular system to increase stroke risk. Thermoregulatory capacity, mediated by the autonomic and cardiovascular systems, becomes less sensitive and effective with ageing. Therefore, in older individuals, extremes of temperature — in particular, cold temperatures —might elicit exaggerated blood pressure responses[69] **[Au: changes to this sentence OK?]**. okThis mechanism could contribute to the increased incidence of intracerebral haemorrhage caused by vascular rupture during the winter months[70].

By contrast, ischaemic stroke, which can be caused by athero-thromboembolism, small-vessel occlusion or cardiac embolism, is associated predominantly with higher temperature and humidity extremes. Exposure to hotter temperatures results in increased cutaneous blood flow and sweating. Volume depletion and activation of the sympathetic system lead to an increased heart rate and cardiovascular strain, which, for individuals with pre-existing cardiovascular disease, can be life-threatening in the context of arrhythmias[71]. In elderly individuals, **[Au: changes OK?] the meaning changed** haemoconcentration (from volume loss) and hypercoagulable states due to increased blood thrombogenic factor concentrations, elevated baseline fibrinogen levels and impaired endothelial function, potentially further elevate the risk of thrombosis[72].

Data on the seasonal risk of venous thrombosis vary **[Au: changes OK?]ok**, with some studies showing increased rates of pulmonary embolism or venous thromboembolism (VTE) during the winter months[66,73-75], some showing an increased incidence of cerebral and venous thrombosis during hotter summer seasons and others finding no association with seasonal changes[76-78]. A systematic review and meta-analysis found an increase in VTE incidence during the winter months overall, but subgroup analyses demonstrated that in hotter climates, VTE incidence was highest in the summer **[Au: changes to this sentence OK?]**[73,74].ok

Increases of core body temperature raise oxygen consumption and metabolic rate, leading to increased heart rate, which, in susceptible individuals with pre-existing cardiovascular disease, could lead to atherosclerotic plaque rupture, causing thromboembolic ischaemic stroke[72]. One study showed that for every 1°C increase in core body temperature, the heart rate increased by 8.5 bpm on average[79]. **[Au: OK to move this sentence to here, to continue the discussion on increased heart rate?]** ok Fluid loss can disrupt levels of electrolytes (particularly potassium and magnesium), which might also precipitate arrhythmias such as atrial fibrillation — a risk factor for stroke.

Severe cases of heatstroke and hyperthermia can result in systemic inflammation and multi-organ failure. At a cellular level, exposure to heat is thought to induce the release of IL-1 and IL-6 from muscles through an exaggerated inflammatory reaction, in addition to intestinal endotoxin release caused by increased gastrointestinal permeability. This combination of events causes leukocyte activation and an inflammatory response; cytokine release promotes a hypercoagulable **[Au: is this what you meant?]ok** state with elevated levels of Von Willebrand factor, tissue factor and thrombin, and reductions in the levels of antithrombin III, protein C and protein S and inhibition of fibrinolysis[80].

Decreased deep body temperature activates the sympathetic and renin–angiotensin system, resulting in vasoconstriction, increased skeletal muscle tone and increased blood pressure, potentially increasing the risk of intracerebral haemorrhage[69]. Hypothermia also induces hypercoagulability owing to increased blood **[Au: OK?]** viscosity, in addition to fluid shifts caused by diuresis, leading to hypovolaemia and clotting abnormalities, which contribute to altered haemoconcentration. Low body temperatures have also been linked to an increased risk of acute myocardial infarction, which was attributed to plaque rupture associated with deposition of cholesterol crystals in plaques[81] **[Au: changes to this sentence OK?]**.

As the findings discussed above illustrate, the mechanisms underlying ischaemic and haemorrhagic stroke are likely to be affected in different ways by extremes of temperature and unseasonal temperatures, highlighting the need for further studies to determine the effects of climate change on each type. **[Au: deletion OK? This statement seemed to come out of nowhere and did not really relate to anything that was discussed above. If you wish to reinstate it, please clarify its relevance to the preceding discussion and provide references to support it]** **please see edits** The basis of acclimatization to the local environment, including possible genetic and childhood environmental influences, needs further exploration, not only to generate better localized public health strategies and locally responsive temperature alert systems, but also, as a co-benefit, to better understand stroke risk mechanisms in general, and to devise short-term acclimatization measures to prepare people, especially those with existing risk factors for stroke, for adverse weather events. **[Au: changes to this paragraph OK, to streamline the text? The original version was quite 'wordy' and difficult to follow in places]**

[H3] Added effects of air pollution. Air pollution and climate change are intrinsically linked, with the burning of fossil fuels producing pollutants while also driving climate change. Data from 68 epidemiological studies involving more than 23 million participants revealed that exposure to the air pollutants $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO and O_3 was associated with an increased risk of hospital admission due to stroke; exposure to $PM_{2.5}$, PM_{10}, SO_2 and NO_2 was associated with increased stroke-related mortality; and exposure to $PM_{2.5}$, SO_2 and NO2 was associated with increased stroke incidence[82] **[Au: changes to this sentence OK?]**. ok Another study demonstrated that long-term exposure to $PM_{2.5}$ was associated with a 24% increased risk of death from cerebrovascular causes and a 13% increased risk of incident stroke[83]. The ELAPSE project found an 8% increase in the incidence of stroke following a 10μg/m^3 increase in long-term NO_2 exposure[84].

Air pollution is known to be associated with stroke **[Au: OK?]ok** risk factors such as diabetes, hypertension and arrhythmia[85-87], but the mechanisms underlying these associations have not yet been fully elucidated. Inflammatory changes triggered by exposure to air pollution could link diabetes and particulate matter exposure[86]. In a study of obese mice, exposure to high levels of $PM_{2.5}$ increased visceral adiposity, insulin resistance and systemic inflammation[88]. Air pollution is also associated with acute changes in heart rate variability in people with existing coronary artery disease[89].

The effects of climate change are likely to be particularly acute for individuals who are already experiencing health and social inequalities that result in increased levels of stress and obesity, adding further to the risk of stroke. Reducing pollution levels will bring multiple health co-benefits that are not limited to the effects on stroke risk. **[Au: changes to this paragraph OK, to streamline the text?]ok**

[H2] Epilepsy

Epilepsy, like stroke, is not a single condition. Although the final common pathway of seizure generation is likely to be shared across the epilepsies, the causes, features, trajectories and multi-morbidity burdens differ widely. Certain rare severe epilepsies, including some developmental and epileptic encephalopathies, are already known to be aggravated by temperature extremes[90]. Other epilepsies, such as frontal lobe epilepsies and juvenile myoclonic epilepsy, could impair frontal lobe function and compromise the planning abilities that are needed to respond and adapt to the effects of climate change[91,92] **[Au: changes to this sentence OK?]ok**. Both interictal epileptiform discharges and seizures might be aggravated by heatwaves even in people with epilepsies that are not generally recognized to be temperature sensitive **[Au: is this what you meant?]**[93ok]. Extreme heat and cold have both been linked to increased hospitalization rates in children with epilepsy, and the effects seem to be aggravated by pollution[94] **[Au: changes to this sentence OK? The cited study explored the effects of both extreme heat and cold]**. ok

Sizeable surveys have shown that people with epilepsy are concerned about climate change, and discussion forums of some epilepsy charities demonstrate marked concern about the impact of heatwaves around the time of their occurrence (Nicola Swanborough and Galia Wilson, personal communications **[Au: please could you provide written confirmation that these individuals have consented to inclusion of this information in the article?]**). Attached to email **[Au: the following text was moved up from a later section, as it seemed to fit better here. Is this OK?]ok** Specifically, in a survey of over 1,000 people with epilepsy and their carers, undertaken by the Epilepsy Society in the UK, after the first of three heatwaves in 2020, 56.1% noted that their seizures were more frequent, more severe or broke through previously established seizure control during the heatwave (Nicola Swanborough, personal communication). Over three-quarters of respondents wanted to see more research into climate change and epilepsy.

[H3] Epidemiology. Preliminary epidemiological evidence and anecdotal information suggest that the effects of climate change will both increase the incidence of epilepsy (for example, through the spread of neurotropic viruses that cause diseases leading to epilepsy[95-99]) and aggravate seizures[100-102] and comorbidities in people with pre-existing epilepsy **[Au: deletion OK, given that hospital admission is addressed in the next sentence?]**. ok Many studies use hospital attendance and admission rates for epilepsy as a measure of the effects of climate change-related adverse weather events and temperature extremes. These proxy measures can provide useful information, as these rates are unusually high compared with other diseases and incur substantial personal and health-care expenses, mostly by people with poor seizure control living in urban areas of high social deprivation — factors that themselves increase vulnerability to the effects of climate change[23,103]. However, these figures might not capture the full picture, as patients and families who are experienced in self-management of epilepsy might not attend hospital following seizures **[Au: changes to this sentence OK, to streamline the text and reduce repetition?]**. ok Moreover, awareness of increased heat vulnerability and weather-health alerting systems might be limited, even among health-care staff[104], and alerts and heatwave plans might be inappropriately structured for this patient group[105].

[H3] Mechanisms. An important mechanism that contributes to seizure generation is dysfunction of ion channels — a class of proteins that show exquisite temperature sensitivity with among the highest Q_{10} values, reaching 4-3–7.0 in temperature-sensing brain structures[106] **[Au: changes to this sentence OK, to avoid an overly long sentence?]ok** . This temperature sensitivity applies to both native channels[107], the activity **[Au: OK?] no, I don't this change is correct; in some epilepsies channels may work perfectly well but be**

disregulated or uncoordinated etc of which is essential for seizure generation of whatever cause, and for mutant channels that characteristically cause many severe types of epilepsy[108]. Therefore, people with epilepsy are likely to be particularly vulnerable to heatwaves and higher temperatures, the effects of which could be compounded by **[Au: changes OK?]ok** disordered thermoregulation[109-112] or sleep disruption from elevated night-time temperatures. Sleep deprivation is an important trigger for seizures in many individuals and is recognized to activate interictal epileptiform discharges **[Au: I deleted the last part of this sentence, as I didn't think it would make much sense to non-specialist readers who are unfamiliar with the complex relationships between sleep and seizures]**[113].ok Antiseizure medications, seizures themselves and interictal epileptiform discharges can all affect sleep quality, adding to the burden of cognitive impairment, daytime sleepiness and behavioural issues that are experienced by people with epilepsy and substantially impairing their quality of life[114]. **[Au: I deleted the last sentence of this section, as its relevance to disease mechanisms was unclear and it seemed to reiterate points made elsewhere in the article]ok.**

[H3] Determinants* [Au: OK? I thought 'importance' was a little vague] *of vulnerability.ok

[Au: I moved the original first sentence of this section to an earlier section — see above]ok

As a general concept, vulnerability is often related to an individual's circumstances, such as occupation, geographical location, deprivation indices and/or specific transient states such as pregnancy **[Au: changes to this sentence OK? I'm not sure that these factors are exclusive to healthy individuals, as the original wording implied]**.ok – changes the meaning, but actually still works In people with epilepsy, vulnerability to environmental challenge **[Au: vulnerability to what? The effects of climate change?]** is often independently conferred not only by the condition itself but also by its commonly associated multi-morbidities[115]. Frailty is common in these individuals[116] and is associated an increased hazard of death[117]. One component of this frailty is **[Au: OK, to provide a clearer link with the previous sentence?]ok** compromised bone health resulting from a combination of causes, including effects of antiseizure medications on vitamin D metabolism; lack of exposure to sunlight; and lack of physical — especially weight-bearing — activity, which increases the risk of sarcopenia and osteopenia. As temperatures rise with climate change, bone health is likely to be further compromised in people with epilepsy because of the increased need to stay out of the sun, thereby reducing **[Au: OK?]ok** vitamin D production and limiting physical exercise. Vitamin D deficiency has been linked to an increased risk of frailty in older people[118].

These multiple strands of evidence all point to an urgent to better understand the risks that climate change poses to people with epilepsy and other disorders of excitability. Research approaches should be sufficiently nuanced to capture the multilayered complexity of the effects of climate change and its downstream consequences **[Au: changes to this sentence OK?]** ok (Box 3). Such work could inform the evolving aims of the WHO Intersectoral Global Action Plan for Epilepsy and other neurological disorders[16], which currently does not contain any reference to climate change.

[H1] Future perspectives

[H2] Imperatives for neurological research

Although the effects of climate change on many neurological conditions are increasingly recognized **[Au: changes OK?]**,ok the need for more research is clear[23], especially with regard to the underlying mechanisms. We need to know which neurological patients will be most vulnerable to environmental stresses under various different climate change projections. In many cases, mechanisms, vulnerabilities and system disruptions might be shared across neurological diseases, enabling efficient transfer of learning from one disease to another (Figure 2). A standardized operational framework for specifying and measuring climate variables and impacts on disease **[Au: a standardized operational framework for what?]** is required, accounting for the many interacting and dynamic complexities that modulate climate change-driven effects on neurological diseases.

Analysis of existing national datasets using artificial intelligence (AI)-based approaches could rapidly generate information and point to solutions, although the carbon cost associated with such projects **[Au: OK?]** will also need to be considered[119-121]. Informative introductions to AI in neurology have been produced[122]. In addition to increasing our understanding of the effects of climate change on the human brain in health and disease, research could also address the psychological basis of engagement with climate change issues and foster this engagement through the design of better messaging[35]. It could also inform practical measures, such as adaptation methods and building construction[123], taking the health-care ecosystems of people with existing neurological conditions into account. **[Au: changes to these last two sentences OK? There was quite a lot of information to digest, so I've tried to present it in a more intuitive way]**ok

Some of the intricate work that is required to understand the consequences of climate change for neurological health might leverage the systems-level integration offered by the practical measure of 'thermal comfort' — the subjective psychological phenomenon of satisfaction with the thermal environment[124]. Thermal comfort is a person-centred measure that can account for many other variables, including local geography. The absence of thermal comfort is a potent driver for both short-term behavioural change[125,126] and longer-term adaptations, such as alterations to the building fabric[127] (for example, retrofitting of insulation **[Au: OK to provide this example?]**)ok or uptake of cooling technologies[128,129]. Personal tolerance to adverse temperatures can be influenced by numerous factors, from genetics and early environmental exposures[134,135] to social[136] and personal norms and practices. **[Au: changes OK? I deleted some of the text, as it seemed quite wordy and repetitive — I didn't think that the general reader needed this level of detail]ok** Formal scales are available to measure thermal comfort[137,138], although in the context of neurological diseases, adaptations to these scales will be needed to account for neurological compromise[139-142], for example, intellectual disability, progressive cognitive and motor impairments, and dysfunction of the mechanisms that mediate appreciation of thermal comfort[143,144] **[Au: changes to this sentence OK?]**.ok In addition, normal thermoregulatory processes might be disrupted in these conditions[145-147]. **[Au: OK to move this information to here? It seemed to be relevant to the discussion on thermal comfort]** Optimization of thermal comfort on an individual basis is an important consideration when designing climate change adaptation strategies for people with neurological diseases **[Au: changes to this sentence OK, to streamline the text?]**.ok, but I don't think mitigation of climate change can work at individual level

Some of the actions that the neurological community can take to minimize the effects of climate change on their patients are summarized in Box 4 and elsewhere[18]. **[Au: changes to this sentence OK?]ok** As discussed in more detail below, reducing the carbon emissions associated with research and health care is an important priority[148]. **[Au: changes to this sentenceOK? The issue of carbon emissions is discussed in the section on creating a sustainable working environment below, so I didn't think that we needed a lot of information here]ok**

[H2] Responding to complexity and continuous change

Neurological diseases are complicated entities that develop in complex environments **[Au: changes OK? I thought that 'complicated entities' already encompassed the complexity of organs and individuals and didn't require further elaboration]**.ok Climate change is altering many aspects not only of the external environment[149,150] but also of the internal milieu[151-153] of the human body in health and disease, as well as of human behaviour. **[Au: deletion OK? These knowledge gaps are addressed elsewhere in the article, and the next sentence seemed to follow on more naturally from the previous sentence]ok** Climate change also threatens biodiversity, the understanding of which has already offered **[Au: OK to use past tense? I'm assuming that the existing treatments can now be synthesized in a laboratory and are unlikely to be threatened by a loss of biodiversity, but you are alluding to the future discovery of new treatments from natural sources. Is this interpretation correct?]** yes, ok important potential treatment options for neurological diseases, such as rapamycin and its derivatives which are used to treat tuberous sclerosis[154], or the viral vectors that are used in gene therapies for epilepsies[155] and early-onset parkinsonism[156]. Projections continue to be generated for climate change, sociodemographic shifts and neurological disease epidemiology[157], but their interrelationships have not been extensively explored **[Au: is this what you meant?]ok**. Although the neurological community is becoming increasingly aware of climate change[15], it still rarely features in neurological disease research and at neurological conferences and meetings.

It is important to consider the temporal and spatial limitations of the currently available data, including the differential effects of climate change in urban versus rural settings **[Au: changes OK? I wasn't sure what you meant by 'urban–rural imbalances']ok**.

Data gathered some years ago, and even in the relatively recent past, might not reflect current climatological features, thereby limiting the extrapolation of longitudinal signals from date-limited cross-sectional studies. The ability of humans to thermoregulate not been well studied in the context of climate change, and many important human brain proteins, especially ion channels, temperature sensors and transporters, demonstrate marked temperature sensitivity. **[Au: deletion OK? This sentence seemed to reiterate a point that had already been made above]ok** A co-benefit of developing thoughtful strategies to address the complex effects of the climate on health, might also be better understanding of disease **[Au: changes to this sentence OK? The original wording was a little vague]**.better?

[H2] Creating a sustainable working environment

Health care accounts for 4–5% of global carbon emissions **[Au: please cite the source of this figure]**: ref: DOI: 10.1016/S2589-7500(23)00229-7 if it were a nation, it would be the world's fifth largest emitter. However, health care systems around the world are taking their responsibilities seriously, with the UK National Health Service, for example, committing to become net zero for scope 1 and 2 emissions **[Au: I have suggested defining 'scope 1, 2 and 3 carbon emissions' in Box 2 — see below]** by 2040 and for all emissions by 2045 **[Au: again, please cite the source of this information] ref: https://www.england.nhs.uk/greenernhs/a-net-zero-nhs/**. Other health-care bodies in Europe, Australia and elsewhere have also been proactive in this area[158-160]. In terms of employing day-to-day low carbon practices and responding to adverse weather events, health-care services in high-income countries might learn from those in low-income and middle-income countries, which have had to practice under these strictures for many years[161].

Medical [Au: OK to specify?ok] research also has a substantial carbon footprint. Our current research model involves the generation, analysis and publication of large amounts of data[162-165], the organization of trials, knowledge exchange through media and at meetings, and a demanding career structure. Each of these steps has a carbon footprint (Table 1 [Au: as we discussed, I have converted this item to a table (see below)])ok that could be reduced [Au: OK, to streamline the text?]ok without compromising scientific endeavour. Reductions in emissions sometimes simply require thoughtful restructuring of the activity in question. For example, the CRASH-2 trial of an antifibrinolytic drug in patients with bleeding trauma achieved a reduction of around 73% in CO_2 equivalents emissions per participant compared with the earlier CRASH-1 trial, largely through faster patient recruitment [Au: OK, to clarify where the savings were made?][166]. ok

Data transfer around the world and the use of machine learning methods for data processing have sizeable carbon footprints, but principled frameworks have been proposed to reduce these emissions[167]. Leading medical journals have issued powerful joint editorials calling for urgent action on climate change, biodiversity loss and human health[168,169], although the carbon footprints of publications themselves have rarely been considered[170-172]. Moving from physical printed journals to digital online journals leads to reductions in carbon emissions and waste[172], as highlighted by a study of dermatology journals[171], but emissions associated with data storage and manufacturing of devices such as tablets, laptops and smartphones are potential confounding factors [Au: OK?]ok that should be considered[170].

The current research career structure typically requires early career researchers to travel to meetings to present their data. These pursuits are enriching but have carbon footprints, and strategies to reduce these footprints have been proposed[173]. In addition, we need to work with funding agencies to ensure that sustainability — like equality, diversity and inclusion and patient–public involvement initiatives — is included in the grant call, application and awards processes, as illustrated by a concordat on environmental sustainability established in the UK[174]. To ensure the relevance and applicability of research generally, but especially in the climate change context, co-creation with affected communities is essential. Individuals can also engage with organizational and institutional programmes that promote sustainability, such as the widely adopted Laboratory Efficiency Assessment Framework[175]. These pursuits can also bring the co-benefit of a better working environments.

[H2] Advocacy and outreach

Clinicians remain trusted sources of information[176], and they have important roles in promoting messaging around climate change and its risks to health — a process that should be considered part of the duty of care[177,178], both to their employers and their patients. **[Au: deletion OK? This sentence seemed to largely reiterate points that were made in the previous sentence, and it's unclear to me why you would consider neurologists to be particularly well placed to advise on issues such as vaccination] we advised DHSC on vaccination issues in people with neurological diseases, but OK** Neurological health-care professionals can take practical steps to inform themselves about how discuss climate change **[Au: OK?]ok** with patients[18]. Regulators have already considered how sustainability might be incorporated into practice[179], and it could also be included in continuing professional development and revalidation processes. In the context of neurological diseases, we need to address how advocacy can be supported for people whose condition itself (for example associated cognitive impairment) presents barriers to the usual approaches **[Au: this statement is rather vague — could you be more specific about the types of approaches and associated barriers that you have in mind?]**[180]. Better?

Engagement with communities with lived experience of neurological disorders will be vital to ensure that daily life continues in the face of climate change and strategies for its mitigation **[Au: changes to this sentence OK, to streamline the text?]**. Increasingly, professional neurological **[Au: OK to specify 'neurological' here?]ok** organizations are increasingly engaging with sustainability and climate change issues[181]. Pro-sustainability actions should become the default option and should bring co-benefits with regard to physical and mental health **[Au: OK to combine and condense these two sentences?]ok**. For people with neurological diseases, customized short-term acclimatization strategies should be considered as a preventative action in advance of serious adverse weather events[182-186], possibly bringing with them co-benfits of improving overall health in these individuals **[Au: changes OK, to streamline the text?]**.

[H1] Conclusions

Overwhelming evidence indicates that the world is rapidly becoming hotter, with serious implications for human health in general and for people with neurological disorders in particular **[Au: changes to this sentence OK?]**. ok Climate anxiety is also prevalent, especially among the young[187]. For neurological and other health-care communities, action on climate change should be considered an element of our daily work.

Formal research exploring the effects of climate change on neurological health is essential. We need to take into account the risks involved and account for the often broad phenotypic spectrum, varied trajectories, comorbidities and pathophysiological complexities of many neurological diseases **[Au: deletion OK? This sentence was very long and difficult** to follow]. Ok Trans-disciplinary engagement involving affected communities, climate scientists, disease specialists, health-care service providers and policymakers will be required.

We should consider ourselves obliged to act now: senior neurological clinicians and neuroscientists can create an atmosphere that permits and promotes discussions about climate change in a professional context, encouraging junior clinicians and early career researchers to participate [Au: OK?]ok. Rather than focusing on either scientific endeavour or the battle against climate change in isolation, we should be aiming [Au: changes OK?]ok to improve neurological health in the context of a changing climate.

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Author contributions

S.M.S. conceptualized the article. M.I.G., S.L. and S.M.S. researched data for the article. S.M.S. wrote the original draft with contributions from the other authors. K. B., D.-J.D., E.M., M.M., A.M., M.T., D.J.W. and S.M.S. reviewed and/or edited the manuscript before submission. M.I.G., S.L. and E.M. prepared the figures. **[Au: changes OK? I have incorporated the information that you provided on our manuscript tracking system when you submitted the article]**

Competing interests

The authors declare no competing interests.

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[Au: as we are publishing this article as a Perspective, we can't include key points]

ok

Supplementary Figure 1 | **[Au: as we discussed, this will now be an online-only supplementary figure]ok** Vulnerability scores of 180 countries to climate change effects compared with age-standardized disability-adjusted life-years (DALYs) and deaths (per 100,000) for all neurological conditions. The x-axis indicates countries (n = 180) for which vulnerability scores are available. The Notre Dame Global Adaptation Index (ND-GAIN) vulnerability score was used to show the propensity of these countries to the negative effects of climate change[188]. The ND-GAIN uses 36 vulnerability indicators across 6 life-supporting sectors: food, water, health, ecosystem services, human habitats and infrastructure **[Au: changes to this sentence OK?]ok**. The figure shows vulnerability scores for 2021 — the most recently published ND-GAIN scores **[Au: please cite the source of the data]**. Ref 188 in current list The vulnerability scores are shown on the left y-axis and DALYs and deaths per 100,000 of population from **[Au: OK here and below?]** neurological conditions, taken from the Global Burden of Disease Study 2021[157], **[Au: OK?]** are shown on the right y-axis. Countries with higher vulnerability scores, such as Somalia, also tend to show higher numbers of DALYs and deaths from neurological diseases than those with lower vulnerability, suggesting that countries with the highest pre-existing burden of neurological conditions will also experience the worst aggravation of those burdens by climate change **[Au: changes OK?]**.ok

Figure 1 | Effects of extreme temperature on the pyloric rhythm of *Cancer borealis*

The crab *Cancer borealis* lives in the Northern Atlantic Ocean, where it experiences temperatures ranging from 2°C to 25°C or more. Animals such as *C. borealis* have evolved many mechanisms to allow them to adjust and acclimatize **[Au: OK?]** okto long-term temperature changes, but extreme temperatures under experimental conditions can cause degradation of neuronal circuit output. **[Au: OK?]** ok The figure shows recordings of the triphasic pyloric rhythm of *C. borealis* in response to acute increases in temperature[27]. The dynamics are complex and unpredictable, probably Eve Marder used 'precisely' and I would prefer to stick with that -it's her work and she is the expert because many interacting channels and other proteins are differently influenced by temperature. **a** | Simultaneous intracellular recordings from pyloric dilator (PD), lateral pyloric (LP) and pyloric (PY) neurons and extracellular recordings from the pyloric dilator, gastropyloric and pyloric motor nerves (pdn, gpn and pyn, respectively) **[Au: changes to this sentence OK?]**. ok At 19°C, the rhythm is regular, but at higher temperatures it is partially disrupted, and at 31°C it shows periods of total silence or 'crash'. **b** | Spectrograms of 220 s at each temperature, showing minor and major disruptions of the regular rhythm as the temperature is increased. **[Au: changes to the legend OK, to reduce repetition? Now that the text has been edited down, I think this item works better as a** figure than a box. Provided that we can obtain the necessary permission, the figure will remain unchanged]ok

[Au: as we agreed, I have converted this item into a box (see below)]ok

Figure 2 | Shared vulnerabilities and system disruptions. Sleep disturbance, stroke and epilepsy share various risk factors and mechanisms that could be affected by climate change-related environmental factors. The figure provides examples of these components. The adverse effects of environmental factors driven by climate change, such as sustained extreme ambient temperatures owing to heatwaves, might have similar characteristics across different brain processes and diseases, affording opportunities for the rapid transfer of learning from one brain process or disease to another. [Au: changes to the legend OK, to reduce repetition?]ok

[Au: as we agreed, I have converted Figure 4 to the table below — please check that all of the information is correct] ok

Table 1 | Carbon footprint of neurological care and research (formerly Figure 4)

Type of activity	**Specific activity**	**CO_2 emissions (kg)**
Air travel to congress	Return flight from Brazil to the UK	7,000
Patient travel to hospital	30 miles in a petrol car (1.4-2.0 litres engine)	20
Brain imaging	Non-contrast brain MRI scan	10
	Brain CT scan	4
Scientific publication	Publication of one manuscript	5
Laboratory analysis for one sample	High-performance liquid chromatography (HPLC)–mass spectrometry	0.251
	HPLC	0.042
Internet use	Processing data and transmitting by internet	0.028–0.063 per GB
	1 MB e-mail	0.020
	Web search that produces five or more results	0.010

The table shows typical carbon footprints of various elements of health-care provision[189,190] and research[191,192] in neurology.

Box 1 | Climate change **[Au: deletion OK? Most of the data in the box are actually from 2023]ok** facts and figures

[Au: I moved the original opening sentences further down the box so that it begins with some more general facts and figures] Since the beginning of the Industrial Revolution in the mid-18th century, energy generation, industry, transport, farming and land-use changes have increased CO_2 levels in the Earth's **[Au: OK?]ok** atmosphere by over 50% ref https://www.climate.gov/news-features/understanding-climate/climate-change-atmospheric-carbon-dioxide and methane by over 150% ef United Nations Environment Programme/Climate and Clean Air Coalition (2022). Global Methane Assessment: 2030 Baseline Report Summary for Policymakers. Nairobi.. We have added 2.2 trillion tonnes of CO_2 to the atmosphere since pre-industrial times ref: https://www.ipcc.ch/sr15/, and levels are higher now than they have been in the last 3 million years ref: https://www.ipcc.ch/report/ar6/wg1/downloads/faqs/IPCC_AR6_WGI_FAQ_Chapter_01.pdf. According to the European Climate Change Service, these anthropogenic greenhouse gas emissions increased the temperature of the Earth by 1.48°C between pre-industrial times and 2023 ref Copernicus: 2023 is the hottest year on record, with global temperatures close to the 1.5°C limit | Copernicus. **[Au: changes to this sentence OK? Please provide references for all of the figures quoted in the opening sentences of this box]** ok Between 1880 and 2023, the 10 warmest years on record have all occurred in the past 10 years[193], with 2023 being the hottest year recorded to date.

Analysis of data from the 2022 heatwave across 35 European countries revealed a sizeable heat-related mortality burden[4], with 61,672 heat-related deaths being recorded **[Au: changes to this sentence OK?]**.ok The highest rates were reported in Italy, Greece, Spain (237), and Portugal (295, 280, 237 and 211 deaths per million, respectively). In the contiguous United States between 2008 and 2017, each additional 'extreme heat day' in a month was associated with 0.07 additional deaths per 100,000 adults[5].

In addition to increased global temperatures, **[Au: OK?]ok** other changes in the Earth's climate system have been observed[194]. Weather patterns have shifted, and extreme weather events such as superstorms, megafloods, severe droughts and unprecedented heatwaves have increased all around the world and are occurring in new, unexpected locations. Uncontrollable wildfires and pollution are also on the increase **[Au: OK?]ok**. Data on the effects of adverse weather events other than heatwaves on human health are limited at present **[Au: is this what you meant?]**.ok

The adverse effects of climate change are unequally distributed across the world[195], and countries with the fewest resources to cope with change — and typically those that have contributed least to global greenhouse gas emissions — are facing the greatest disruption. The burden of neurological diseases is also unequally distributed. The geographical overlaps and projected trajectories of the dynamics of disease burden, disease-related deaths and climate vulnerability are illustrated in Supplementary Figure 1. Notably, the distribution of current research linking climate change and neurological diseases does not match the pattern of greatest burden[23].

Box 2 | Climate change terminology **[Au: changes to this box OK, to conform to our standard box format? I didn't think that it was necessary to provide reference, as these are all fairly standard definitions]ok**

Air pollution

Changes in the properties of the atmosphere caused by chemical, physical or biological agents. Common pollutants include particulate matter, carbon monoxide, nitrogen dioxide and sulfur dioxide.

Biodiversity

The diversity of life within a given area or region. Varies owing to evolutionary history, climate, environmental factors and the effects of human activity.

Carbon footprint

A measure of carbon-related greenhouse gas emissions from a particular person, organization, product or activity.

Climate

The average weather conditions, including temperature, precipitation and wind, in a particular area.

Climate change

Measurable changes in the climate of an area or region, such as a shift in the average measured climate baseline and/or more extreme weather conditions. Hazards associated with climate change include heatwaves, droughts, water scarcity, wildfires, flooding and storms, along with melting polar ice, rising sea levels and biodiversity loss.

Climate change adaptation

A range of actions aimed at reducing vulnerability to the effects of climate change, including sea defences, fresh water storage, building adaptation, wildfire management, education and improved health-care provision.

Climate change mitigation

Actions taken to decrease or avoid greenhouse gas emissions, such as reducing fossil fuel consumption, switching to renewable energy, increasing energy efficiency, reforestation and rewilding.

Climate change vulnerability

The degree to which system or people are susceptible to the adverse effects of climate and environmental stressors, including temperature increases, changes in the frequency and intensity of precipitation and extreme weather events.

Climate crisis

The crisis caused by unchecked climate change and characterized by increased global temperatures, extreme weather events, ocean acidification and coral bleaching, food and water insecurity, health hazards and economic deterioration or displacement.

Climate resilience

The capacity of a society or environment to manage and minimize the effects of climate change. Examples include training people to acquire new skills and diversify household income sources, building stronger disaster response capacities, and improving climate knowledge and early warning systems.

Climate seasonality

Seasonal cyclical changes in temperature and precipitation that occur over the course of a year, for example affecting soil moisture levels, snow cover, evaporation rates, river flows and lake levels.

Extreme weather events

Meteorological events such as heatwaves, floods and droughts that have become more frequent and/or more intense or occur in regions where they have rarely appeared in recorded history. Examples might include heatwaves, floods or droughts thought to be very unlikely to have occurred, or been as severe, without climate change.

Global mean air surface temperature

The global average near-surface air temperatures over both land and oceans. According to this measure, 2023 was the hottest year on record (likely to be replaced soon by 2024).

Global warming

The increase in the Earth's average surface temperature caused by an increase in the concentration of greenhouse gases in the atmosphere. The current warming trend is advancing at an unprecedented pace.

Greenhouse gases

Gases that trap heat from the sun in the Earth’s atmosphere. Examples include water vapour, carbon dioxide, methane and anaesthetic gases such as desflurane.

Heatwave

A locally defined prolonged period of excessively hot weather conditions, often accompanied by high humidity. Heatwaves have become more frequent and more severe with climate change. Both heatwaves and cold snaps (rapid drops in temperature) could have health consequences.

Scope 1, 2 and 3 carbon emissions

[Au: please provide a brief definition] Scope 1 are emissions owned or controlled by an organisation. Scope 2 covers indirect emissions from the purchase and use of electricity,

steam, heating and cooling. Scope 3 includes all other indirect emissions that occur in the upstream and downstream activities of an organisation.

Weather

The state of the atmosphere, including temperature, cloud cover, wind, humidity, precipitation and atmospheric pressure, at a particular time in a specific location.

Wet bulb temperature

The temperature at which air reaches saturation without a change in its heat content. This measure is important for human thermal comfort and human activity.

Box 3 | Climate change vulnerability in people with epilepsy **[Au: this item was adapted from the original Figure 2 — please check that all of the information is still correct]** **ok**

Factors that contribute to climate change vulnerability

- Stress, sleep deprivation and pre-existing increased risk of sudden unexpected death in epilepsy (SUDEP).
- Cognitive impairment, poor mental health and/or intellectual disability.
- Pregnancy.
- Frailty.
- Very young or very old age.
- Comorbidities of epilepsy,
- Effects of antiseizure medications on thermoregulation, sleep and vitamin D metabolism.
- Inequitable access to health care and/or disruption to supplies.

Adaptive measures

- Increasing public awareness of risk with appropriate messaging and systems.
- Addressing socioeconomic deprivation.
- Improving residential housing and access to green spaces.

Benefits and co-benefits of adaptive measures

- Reduced number of seizures.
- Improved sleep and quality of life.
- Decreased risk of SUDEP.
- Reduced climate anxiety.
- Fewer hospital admissions, resulting in cost savings for health services.
- Greater access to public transport and appropriate housing.
- Greater public awareness of risks, leading to increased climate action and improved health.

Box 4 | Practical steps for neurologists

Setting standards for sustainability in professional life

- Research activity: measure and understand the effects of extreme temperatures, determine the effects of climate change on your own practice, devise sustainable research, trial designs and data collection strategies, and publish manuscripts in open-access online journals where possible. **[Au: changes to this point OK?]ok**
- Participate in organizational and corporate programmes that promote sustainability.
- Meetings: attend online where possible or promote more sustainable engagement, such as travelling by train rather than flying, consuming plant-based healthy food and organizing hybrid meetings. Lobby for more sustainable behaviours and options at meetings.
- Engage with your team, particularly early career researchers, to promote climate change discussions, and encourage them to explore the effects of climate change on people with neurological diseases, learn more about sustainability, inform patients about the effects of climate change, and adopt sustainable practices **[Au: OK?]ok**, such as travelling by foot or bicycle where possible and consuming plant-based healthy food at work meetings.

Engaging patients and their families or carers

- Provide information about the effects of climate change.
- Regularly review medications and reduce the number where possible. **[Au: changes to this point OK?]ok**
- Explore the possible effects of extreme temperatures and other adverse weather events with patients to understand their vulnerabilities.
- Ensure that people with known temperature-sensitive conditions or with existing or latent autonomic dysfunction are aware of the possibility of disordered thermoregulation and vulnerability to extreme temperatures.

- Recognize and help patients with climate anxiety, for example, by encouraging engagement in practical sustainability activities, which have co-benefits for mental health and the environment.
- Promote awareness of appropriate storage of medications, especially during heatwaves **[Au: OK?]**.ok
- Inform patients about staying cool during uncomfortably hot nights **[Au: changes OK, to streamline the text?]ok** to permit good quality sleep, and discuss the value and meaning of national and local weather-health alerting **[Au: OK, for consistency with the main text?]** oksystems.
- Provide information about plant-based diets and more thermally comfortable homes, including planning for a hotter future.