Impact Of Global Warming On Brain Temperature

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Abstract

Objective: Very few studies have looked into the direct effects of environmental temperature on human health. The direct impact of global warming on human brain temperature, behaviour and disease burden was studied in a variety of neurosurgical conditions in the National Hospital for Neurology and Neurosurgery from June 2022 onwards.

Methods: In this single-centre prospective observational study, data was collected from patients with an indwelling M.Scio ventricular shunt sensor reservoir for various illnesses, as out-patient clinic appointments during summers. Demographic data (age, sex), past medical history, history of incidents of ill health/relapses requiring medical assistance, history of medication, symptoms at presentation, neurological assessment and baseline vitals will be recorded. Only healthy patients with no acute symptoms of illness were included. The temperature, humidity and carbon dioxide concentration of the clinic room was recorded using HOBO MX CO_2 . The brain temperature and ICP was recorded in lying, sitting and standing positions using M.Scio ventricular shunt sensor reader unit. Patients were asked survey questions focusing on subjective feelings of wellness, heat-tolerance, any noticeable behaviour changes and objective incidents of illness requiring medical attention. The same patients were seen again in out-patient clinics during winters and same information and measurements were repeated and recorded. The results were compared for the different seasons in individual patients. Comparison of two groups of patients (rise in brain temperature vs maintained core-brain temperature) was done by two sample t-test using SPSS (version 25.0, IBM).

Results: After exclusions, brain temperature was measured in 54 patients during both summers and winters (average age 41 years; male:female 15:39. [n=18, hydrocephalus; n=8, idiopathic intracranial hypertension; n=6, Chiari malformation; n=5, CSF leak; n=10 haemorrhage; n=3, intraparenchymal brain tumour; n=4, cerebral infection). The room temperature during the summers (average 27.5 – 29.5°C), was an average 2 - 3°C higher than during winter (average 24.5 -26.5°C). Room humidity and CO_2 conc was comparable in both seasons. 34 patients had an increase in brain temperature of 0.7 – 2°C during summer as compared to winter ($p < 0.0001$). The average ICP was higher in all individuals during summer (average 2-6mmHg). Patients cohort depicting rise in brain temperature with environmental temperature also had >3 incidents of ill-health/disease-relapse/hospital admissions during summers.

Conclusion: Thermoregulation in humans may not be as well-controlled as previously believed. Global warming is likely to have a direct effect on human brain temperature and the presentation of neurological diseases. This is an ongoing study and validation of the results will be required with larger cohorts.

Introduction

Global warming and climate change have been recognised as a threat to life on Earth since the 1800s[1]. In 1824, Joseph Fourier calculated that an Earth-sized planet, at our distance from the Sun, ought to be much colder[1]. In the 1860s, physicist John Tyndall recognized Earth's natural greenhouse effect and suggested that slight changes in the atmospheric composition could bring about significant climatic variations[1]. This led to the establishment of global records of surface temperature in 1882[2]. In 1896 Prof Svante Arrhenius first coined the term 'Global Warming' and predicted that changes in the level of atmospheric carbon dioxide could alter earth's surface temperature through the greenhouse effect[3]. Previously, the average global surface temperature of the 20th century was calculated to be 13.9°C, but in the 143-year record, the ten warmest years have all occurred since 2012 and 2022 has established a new global temperature record with an increase of 1°C in the average global surface temperature[2].

Several studies have investigated the detrimental impact of global warming on crop production[4, 5], fresh-water and marine life[6, 7], with all models projecting an inversely proportional effect of rising temperature on crop and aquatic-life survival[4-8]. The effect of subsequent water and food shortage on human populations has also been investigated, with models indicating that the situation will get progressively dire with each 0.5°C increase in global temperature[4, 8]. It is expected that cost of living will increase drastically for temperature increase of 1.5-2°C, with more loss of labour, and more frequent heat-waves and adverse climate events[9-11].

Few studies have evaluated the impact of climate change on human thermoregulation[12, 13]. These studies have focussed on the identification of vulnerable individuals with possible compromise of thermoregulatory mechanisms due to chronic dermatological illnesses impairing efficient sweating and heat conduction[13] or have suggested behavioural adaptations to aide survival by altering sleep/wake cycles towards a sub-nocturnal pattern for outdoor activities, to avoid day-time heat[12]. Even fewer studies have explored the direct effect of the increasing temperature on illnesses[14] and mortality[11, 15] in humans. These studies observed the detrimental effect of rising temperature on the incidents of neurological illnesses such as Parkinson's disease and cardiovascular disease in humans[14], as well as the mortality burden of heat-stroke related deaths[11, 15].

The brain is the amongst the most metabolically active organs in the human body. During awake yet resting conditions, brain metabolism takes up 15 percent of total body metabolism[16]. This figure can increase to 150 percent with superfluous brain activity[16]. Since basal metabolic rate is a significant factor for heat production, along with additional metabolism due to muscle activity and increase in metabolic rate due to effects of adrenergic hormones and thyroxine, the human brain is also amongst the most exothermic organs of the body[16]. Like most other body cells, the metabolic rate of neurons further increases due to extra chemical activity brought upon by increase in neuronal temperature[16], further increasing the temperature of the brain. This makes the brain especially susceptible to heat injury and the possibility of entering a vicious cycle leading to heat-stroke. Consequently, the brain contains two thirds the quantity of heat-sensitive thermostatic temperature sensors as compared to cold-sensitive sensors[16]. These sensors play crucial role in the thermo-regulation of the body and protecting the brain from heat-injury.

In addition to its endogenous heat, exogenous heat is also transmitted to the brain through blood from skin, deep body viscera and the great veins[16]. This is of prime significance with rising global temperatures and frequent heat-waves. Cerebrospinal fluid (CSF) is formed by the choroid plexus, ependyma, blood capillaries of the blood-brain barrier (BBB) and brain parenchyma, through ion and glucose transporters and aquaporins[17-19]. Studies using biological dyes and neuroimaging have revealed that there is a continuous mixing between brain's interstitial fluid, secretions of blood vessels and CSF, as well as a continuous pulsatile flow of CSF in synchrony with the cardiac and respiratory cycles in addition to the unilateral flow maintained through a hydrostatic gradient[17, 19-22]. This allows for exceptionally efficient system of heat conduction from both the brain parenchyma as well as the blood through the BBB into the CSF.

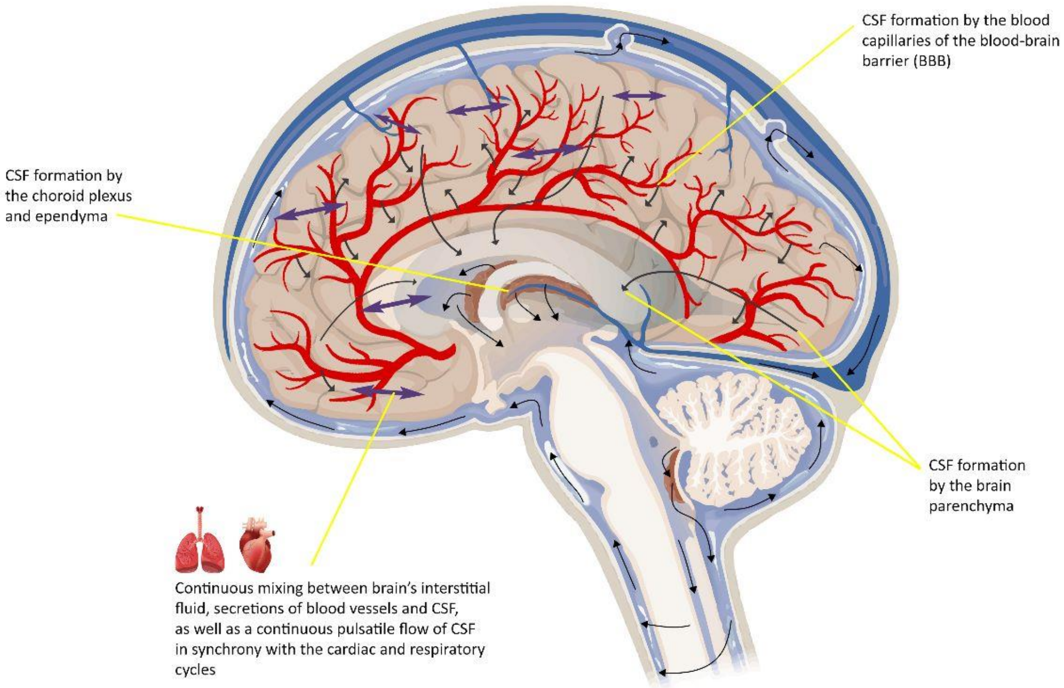

Fig 1. The mechanisms of CSF formation and mixing deem it an exceptionally efficient system of heat conduction from both the brain parenchyma as well as the blood through the BBB, making CSF temperature an accurate reflection of both central and peripheral core temperature.

Thus the temperature of the CSF is an accurate reflection of both central and peripheral core temperature. CSF is absorbed into the venous circulation through the arachnoid villi, nasal lymphatics, perivascular and intramural pathways of blood vessels of the brain, forming the so-called glymphatic circulation in a continuous pulsatile manner[18, 20, 22]. The anterior-hypothalamic and pre-optic area of the hypothalamus senses the temperature of the CSF through special sensory neurons and sends signals to the posterior-hypothalamus which triggers the thermoregulatory mechanisms of the body either via vasodilation, sweating, and slowed metabolism or by vasoconstriction, piloerection, shivering and increased metabolism depending on the temperature of the CSF respectively[16]. This is also associated with behavioural change[16].

The continuous pulsatile flow of CSF in synchrony with the cardiac and respiratory cycles can be studied as part of the intracranial pressure (ICP) waveform. The ICP waveform has 3 peaks. The first corresponding to increase in CSF pressure as a result of rise in arterial pressure with cardiac systole. This is followed by the second peak resulting from the subsequent rise in ICP, reflecting intracranial compliance. The final peak corresponds to the closure of the aortic valve and the rise in CSF pressure resulting from it. ICP pulsations from the cardiac cycle are faster and are superimposed on the slower waveform arising from the respiratory cycle[23-26].

Recently, ICP waveform can be studied telemetrically through ventricular shunt sensor reservoirs[27]. These reservoirs are housed with a measuring cell which is located directly above the entry point of the ventricular catheter into the sensor reservoir. As a result, CSF enters the sensor reservoir with each stage of the cardiac cycle, depicting the ICP peak during that stage, and the drop in ICP with diastole and subsequent CSF displacement, which is precisely recorded by the measuring cell and the ICP waveform is accurately quantified.

Fig 2. ICP waveform can be studied telemetrically through ventricular shunt sensor reservoirs housed with a measuring cell located directly above the entry point of the ventricular catheter into the sensor reservoir.

The direct impact of environmental temperature on human brain temperature, thermal comfort, behaviour and disease burden was studied in a variety of neurosurgical and neurological conditions, in the National Hospital for Neurology and Neurosurgery from June 2022 onwards, as part of a Greener NHS plans approved service evaluation, through an M.Scio ventricular shunt reservoir sensor, which allows for simultaneous measurement of intracranial pressure (ICP) and brain temperature.

Methodology

Study design: A single-centre prospective observational study was performed on all patients in The National Hospital for Neurology and Neurosurgery from June 2022 onwards, who had an M.Scio ventricular shunt sensor reservoir (MIETHKE M.scio® - B. Braun Medical Ltd) in-situ for various neurosurgical and neurological illnesses, as part of out-patient clinic appointments during hot summer days. Demographic data (age, sex), past medical history, history of incidents of ill health/relapses requiring medical assistance, current and previous medication, symptoms at presentation, neurological assessment and baseline vitals were recorded. The temperature, humidity and carbon dioxide concentration of the clinic room was continuously recorded using HOBO MX CO2 (HOBO®Onset Computer Corporation, UK) data loggers. The skin temperature of the patients was recorded using infrared thermometer (Tri-TempTM, TriMedika, Belfast). The brain temperature and ICP of the patients was recorded in lying, sitting and standing positions using M.Scio ventricular shunt sensor reader unit (MIETHKE M.scio® - B. Braun Medical Ltd).

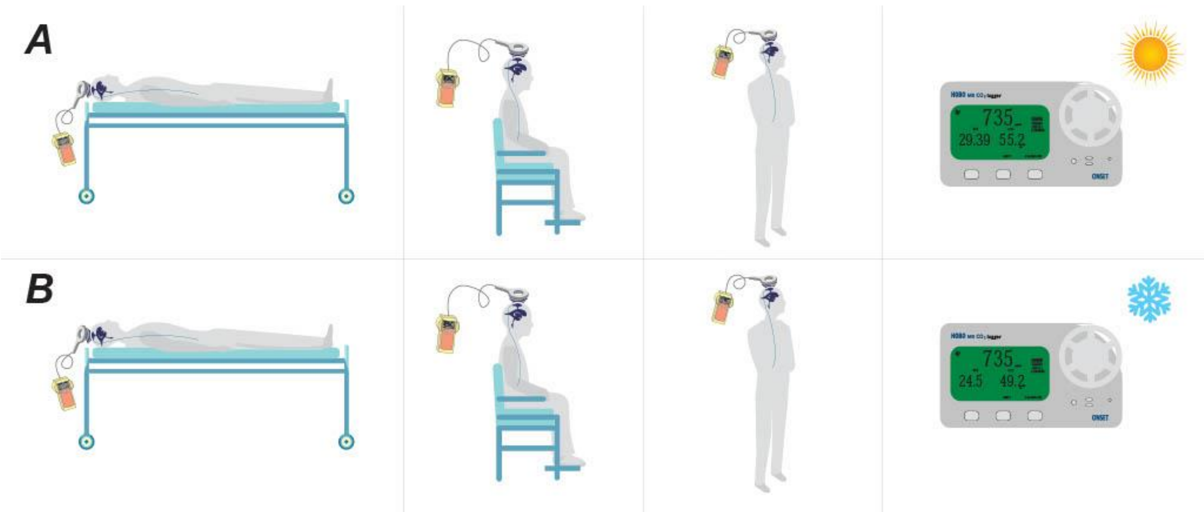

Fig 3. The brain temperature and ICP of the patients was recorded in lying, sitting and standing positions using M.Scio ventricular shunt sensor reader unit. The temperature, humidity and carbon dioxide concentration of the clinic room was continuously recorded using HOBO MX CO2. The data is recorded in the same individual in the same manner during both summers (A) and winters (B).

During the clinic appointment, patients were asked survey questions focusing on subjective feelings of wellness, heat-tolerance, any noticeable behaviour changes such as moving to a more comfortable environment, any noticeable increase in irritability, anger or aggression and objective incidents of illness requiring medical attention. The patients were seen again in out-patient clinics during winters and same information and measurements were repeated and recorded in the same manner. These results were compared for the different seasons in individual patients.

Inclusion criteria: All patients with an M.Scio ventricular shunt sensor reservoir in-situ for various neurological and neurosurgical conditions who were revealed to be healthy on neurological assessment, baseline vitals assessment, review of medical and drug history and presented with no acute symptoms of illness.

Exclusion criteria: Patients with an M.Scio ventricular shunt sensor reservoir in-situ, found to be currently/acutely unwell at the time of review in clinic.

Patients with malfunction/under-function of whole or part of the shunt system.

Stable patients with concomitant intracranial pathology potentially interfering with the results (example: untreated tumour).

Patients residing abroad and unable to attend the clinic appointment.

Ethics and Research Governance: The study is conducted as part of approved service evaluations (Service environments with respect to Greener NHS plans - 62-202122-SE; Health related experience of climate change - 63-202122-SE).

Statistical analysis: Comparison between the two groups of patients (rise in brain temperature with increased environmental temperature vs maintained core-brain temperature) was done by two sample t-test using SPSS (version 25.0, IBM).

Results

Patient characteristics: After exclusions, brain temperature was measured in 54 healthy patients during both summers and winters with average age of 38 years (range: 22-79), 72% (39/54) were younger than 45 years; male:female 15:39; 37% (20/54) patients were obese (Body Mass Index >30). 18 patients had hydrocephalus, eight patients suffered from idiopathic intracranial hypertension (IIH), 6 patients had ventriculoperitoneal shunt (VPS) inserted secondary to Chiari malformation, 5 patients had VPS inserted secondary to CSF leak, 10 patients had past medical history of intracerebral haemorrhage and 3 patients had past medical history of intraparenchymal brain tumour. Four patients had shunt inserted following the development of cerebral infection.

Total number of participants	54
Average age (years)	38
M:F	15M:39F
Percentage obese	37%
Hydrocephalus	18
IIH	8
Chiari malformation	6
CSF leak	5
Intracerebral haemorrhage	10
Brain tumour	3
Cerebral infection	4

Table 1. Patient characteristics

Intrapersonal variations in brain temperature relative to environmental temperature: 34 patients showed an average increase in brain temperature between the range of 0.7 – 2°C during summers as compared to winters. On a paired t test the result was found to be extremely statistically significant ($p < 0.0001$). 59% (28/34) of these patients had a rise in brain temperature between 1.5-2°C. 20 patients did not show significant change in brain temperature between the seasons ($p = 0.5373$).

Intrapersonal variations in intracranial pressure relative to environmental temperature: The average ICP was higher in all individuals during summer (average 2-6mmHg) as compared to winters, regardless of seasonal variation in brain temperature. Patients who demonstrated concurrent rise in brain temperature during summer had more pronounced rise in ICP during summer, and landed on the higher end of the range. On a paired t test the result was found to be extremely statistically significant ($p < 0.0001$).

Association between brain temperature and ICP: Brain temperature readings showed very minute changes in parallel with the ICP readings in all individuals. During any particular season, the brain temperature remained constant in the whole number but showed rise or fall in the decimal value with rise or fall in the ICP respectively.

Seasonal variation in room temperature, humidity and carbon dioxide concentration: The room temperature during the summers (average 27.5 – 29.5°C), was an average 2 - 3°C higher than during winter (average 24.5 -26.5°C). Carbon dioxide concentration was comparable in both seasons, and <2% increase in room humidity was observed during summers.

Seasonal variation in baseline vitals: 15 patients showed a 0.4 – 0.9°C rise in skin temperature during summers. 39 patients did not show change in skin temperature relative to environmental temperature. Heart rate and blood pressure were comparable during both seasons in all the participants.

Subjective feelings of wellness: All the patients demonstrating rise in brain temperature with environmental temperature expressed subjective feelings of restlessness, loss of focus and impaired cognition. 15 of the 34 patients expressed feelings of chest tightness and inability to breathe efficiently, which was not reported by any of the normo-thermic brain cohort ($p < 0.0001$).

Incidents of ill-health/disease-relapse/hospital admissions during summers: Patients cohort depicting rise in brain temperature with environmental temperature also had >3 incidents of ill-health/disease-relapse/hospital admissions during summers. 23 out of the 34 patients displaying increase in brain temperature with increased environmental temperature suffered from vascular headaches, of these 22 reported increased frequency and severity in migraine in summers, along with increased episodes of vasovagal attacks. 5 patients suffering from seizures reported increased incidents of relapse requiring increased medicinal demand. Patients capable of maintaining core brain temperature reported ≤ 1 incidents of ill-health/disease-relapse/hospital admissions during summers ($p < 0.0001$).

Heat-intolerance: 52 participants reported feeling more comfortable in cooler weather.

Behavioural change: 35 patients (34 showing rise in brain temperature and 1 maintaining core-brain temperature) reported changing rooms, sitting in air-conditioning and avoiding leaving the house in summers ($p < 0.0001$).

Increased irritability, anger or aggression: All 34 patients with seasonal brain hyperthermia reported increased anger, irritability and aggression during summers. This subjective patient feedback was confirmed by the partners and family members accompanying the patient in clinic. Patients maintaining core brain temperature did not report increase in irritability, anger or episodes of aggression ($p < 0.0001$).

Influence of demographics: Age and gender had no impact on the observed results, which seemed to be uniformly distributed throughout all ages and both genders ($p = 0.2939$).

	Number of patients	Average range	p-value	Present
Rise in brain temperature during summers (RBTs)	34	0.7 – 2°C	$p < 0.0001$	YES

Rise in ICP during summers	54	2-6mmHg	p < 0.0001	YES
Seasonal variation in room temperature	N/A	2 - 3°C	p < 0.0001	YES
Seasonal variation in room humidity	N/A	< 2%	p = 0.5423	YES
Seasonal variation in room carbon dioxide concentration	N/A	N/A	N/A	NO
Seasonal variation in skin temperature	15	0.4 – 0.9°C	p = 0.0327	YES
Seasonal variation in heart rate	0	N/A	N/A	NO
Seasonal variation in blood pressure	0	N/A	N/A	NO
Subjective feeling of poor wellness	34 RBTs	restlessness, loss of focus, cognitive impairment, chest tightness, difficulty breathing	p < 0.0001	YES
Incidents of ill health requiring medical intervention	34 RBTs	> 3	p < 0.0001	YES
Heat intolerance	52	N/A	p = 05192	YES
Behaviour Change	35 (34 RBTs + 1)	seeking shelter from heat	p < 0.0001	YES
Increased irritibility,	34 RBTs	N/A	p < 0.0001	YES

anger,
aggression

Table 2. Results

Discussion

Principal findings and literature review: To the best of our knowledge, this single-centre study represents the first of its kind exploring the direct impact of global warming on the brain temperature and nervous function of human beings.

The study demonstrated increase in brain temperature in response to increase in environmental temperature beyond that which can be explained by normal physiological ranges. The textbook of medical physiology deems a rise in core brain temperature beyond 0.6°C as pathological[16]. All the patients in our studied cohort that demonstrated increase in brain temperature in response to global warming, (63%, n = 34/54) ,displayed rise in brain temperature in the range of 0.7 – 2°C, thus indicating pathological function. This was coupled with a raise in ICP in these individuals beyond normal parameters. Patients displaying rise in brain and body temperature during the heat-wave also reported greater than 3 incidents of ill-health/disease-relapse during summers and in hot climates, such as during vacationing in hot countries, warranting medical attention and incidents of hospitalisation. Parallel observations made by the neurology team in our centre, looking at the seasonal variation in the frequency of epileptic seizures in context of global warming, found that the frequency of seizures in epileptic patients sharply increases during summers. This is in keeping with a study performed by Kim et al in which rise in brain temperature of 1°C through application of micro-magnetic frequencies led excitation of neurons[28]. This can also be reflected by the seasonal variation in the quantity of acute neurosurgical referrals, with an increase in neurosurgical referrals during summers[29]. These patients also reported having feelings of increased anger, irritability and short-temperedness during hot weather with few reporting incidents of aggression. This is also depicted by the five-fold increase in the overall number of trauma referrals in a major trauma centre in England, with a combined 14% escalation in assault and non-accidental injuries from 2011 to 2018, and a sharp rise in incidents during heat-waves[30]. In 2011 Cook et al analysed 1 year data of NHS Direct England and found that the highest load for adult referrals were for symptoms of mental health, and that this was particularly significant during the few months leading on from July[31], thus begging the question if global warming has a direct impact on human brain.

It was also observed that during a particular season, the brain temperature reading of an individual showed very minute changes in parallel with the ICP waveform. The brain temperature increased and decreased in the decimal value with each peak and dip in the ICP waveform respectively, while the whole number for the brain temperature remained unchanged. This can be explained by the mechanisms of CSF formation and hydrodynamics. CSF is continuously conducting heat from the brain, and with each cardiac systole a greater quantity of warm CSF enters the shunt reservoir with the associated rise in ICP. As this CSF dissipates it washes away the heat from the brain leading to some degree of cooling. This runs in parallel with decrease in ICP evident by cardiac diastole and decreased arterial pressure. Thus it can be hypothesised that CSF may act as a coolant for the central nervous system.

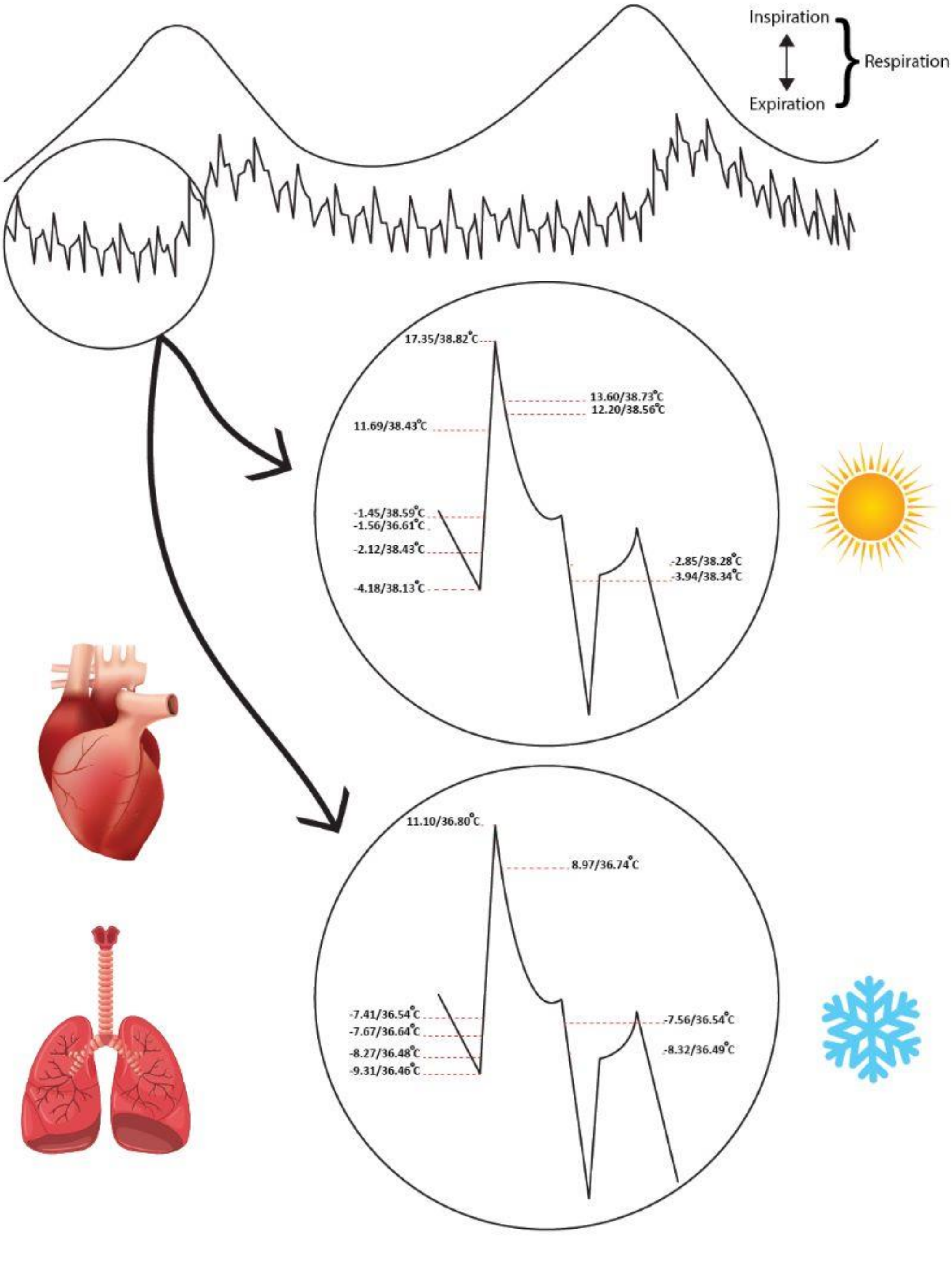

Fig 4. Brain temperature reading showing very minute changes in parallel with the ICP waveform. Temperature rises with rise in ICP and vice versa.

The data also showed that 67% of the patients showing rise in brain temperature with global warming, suffered from migraines and vascular headaches and of these 95% also endured concomitant vasovagal attacks. This may point towards autonomic and thermoregulatory dysfunction in individuals incapable of maintaining core brain temperature with rise in environmental temperature.

The M.scio, is already in clinical use for ICP measurement, however, it's use to observe brain temperature as a function of Global Warming is novel. The temperature and pressure measurement is carried out by means of a measuring cell located directly above the entry point of the CSF through the ventricular catheter inside the body of the M.Scio sensor reservoir. The measuring cell is enclosed in a titanium housing which protects it against external influences thus ensuring the reading of the M.Scio is not influenced by the overlying skin and provides high functional reliability. To achieve high accuracy in temperature measurement, the M.scio is calibrated during the production process. This involves systematically applying numerous temperatures and pressures in a chamber and correlating the readings with these parameters, ensuring compensated temperature dependence of the sensor with changing body temperature and pressure. The brain temperature values of the M.scio can be measured using the Reader Unit Set. The readings are display and automatically saved with date and time on an SD card. For a later detailed analysis and research purposes, the data and curve progressions can be called up again with the Reader Unit Set or analysed with ICPicture. Thus making it possible to accurately measure brain temperature in patients with M.Scio sensor reservoir in-situ.

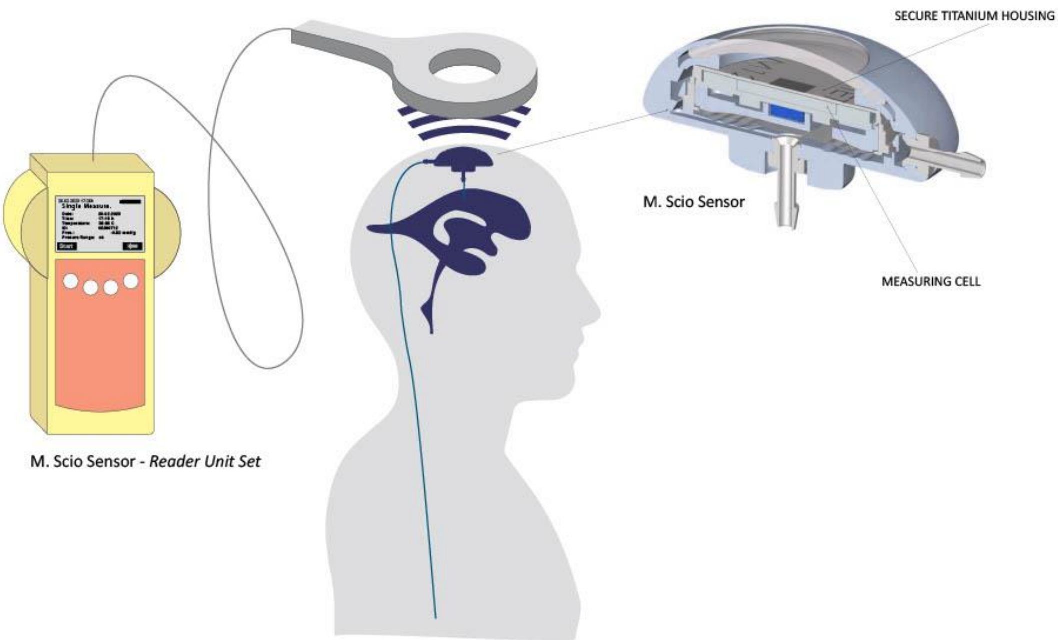

Fig 5. The titanium housing of the measuring cell protects it against external influences thus ensuring the temperature reading of the M.Scio is not influenced by the overlying skin and provides high functional reliability.

Impact and potential benefit: Climate change has now become an immediate threat to life on Earth. Countries have debated how to combat climate change since the early 1990s. These negotiations have produced several important accords, including the Kyoto Protocol and the Paris Agreement[32], but the Earth's average temperature is continuing to rising at an unprecedented rate, leading to more intense heat waves, floods, droughts and species loss. Our study hold great impact in being the first of its kind to explore the result of rising global temperatures on brain temperature of human beings and its link to increased incidents of illness and behavioural upset. This study may show that cerebral thermoregulation in humans is not be as well-controlled as previously believed. In the context of global warming, possible effects on human brain temperature and neurological diseases needs more attention, and therefore this study holds significant value. The results can motivate people to make more effort to prevent global warming and promote sustainability, thus benefitting the entire humanity. It can also feed into further research paving way for the potential development of pharmacological therapy to control brain temperature and associated neuronal activity thus protecting vulnerable individuals.

Conclusion

Global warming may have a direct impact on human brain temperature, leading to increased morbidity and mortality of susceptible individuals. The information obtained has the potential to challenge our understanding of human thermoregulation, vulnerability to global warming and risk to health and life with rising environmental temperatures. It may encourage us to prevent morbidity and mortality in vulnerable individuals by making more of an effort to prevent global warming. This is an ongoing study and validation of the results will be required with larger cohorts.

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Supplementary data:

Printed questionnaire on the