

Evidence of Climate Change Impact on Parkinson's Disease

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Abstract

We have investigated the link between climate change and Parkinson's diseases (PD) by contrasting variations between 1990 and 2016 of PD patients' indices (prevalence, deaths, and disability-adjusted life years) and climate indices (warming and annual average temperature) for 185 countries. Countries have been clustered in four categories, depending on whether they had higher-than-median warming and higher-than-median temperature, and for each cluster variations in PD patients' and climate indices have been studied. In the cluster of the 25 countries (home to about 900 million people) characterized by higher-than-average warming and higher-than-average temperature, we have found evidence of a correlation between more intense warming and higher variations. This statistical result is discussed and linked to other evidence reported in literature. To our knowledge, this is the first time that a statistically-sound link between climate change and the epidemiological data of PD patients has been found and documented.

Parkinson's Disease And Climate Change

The Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder characterized classically by tremor, bradykinesia-akinesia, rigidity and balance deficit, and eventually by depression, cognitive and neurovegetative dysfunctions (Kalia and Lang, 2015). In 2016, PD worldwide affected more than 6 million subjects, while they were only 2.5 million in 1990, mainly because of an increase in the number of elderly people, with potential contributions from longer disease duration and environmental factors (Dorsey et al., 2018; Feigin et al., 2019). Among the environmental factors, climate change resulting in global warming (IPCC 2018, 2019) plays a pivotal role.

From such premises, an important question is whether there is any evidence that climate change can lead to an increase in PD cases. If this is the case, we should expect that countries with highest temperature increases have an enhanced prevalence of PD. Human beings as living endothermic organisms have indeed several features that can compensate for temperature changes, which are however altered in elderly or sick people (Grosiak et al., 2020). In particular, PD patients may exhibit a spectrum of thermoregulatory dysfunctions, which can be exacerbated by heat stress and heat waves (Coon et al., 2020). Although the increase in PD prevalence is well documented by literature reports (Vos et al., 2020), the link between global warming and the enhanced PD prevalence remains elusive. To our knowledge, it has not yet been reported a relationship between the mean temperature in these last years and the prevalence of neurodegenerative diseases. This could be due to the difficulty or inappropriateness of collecting data (considering the quality of life in most poor world countries); moreover, data are still too recent and there is too much variability.

Dorsey et al. (2018) listed the global, regional, and country-specific variations, between 1990 and 2016, of 3 epidemiological indices related to PD patients: prevalence, deaths, and disability-adjusted life years (DALYs). They reported an increase in all 3 indices, and concluded that 'the global burden of PD has more than doubled'. Starting from Dorsey et al., and contrasting their PD data with climate data covering the

same period (1990-2016), we aim to assess whether there is any relationship between the 1990-2016 PD patients' epidemiological variations and climate change-induced warming. Since we would expect that global warming could have a major effect on warmer countries, we have decided to compute, for each country, two climate indices: the warming between 1990 and 2016, and the country average temperature in 2016 as indicator of each country's climate. Standard, robust statistical methods are going to be applied to assess whether diachronic PD patients' epidemiological variations are more evident in warmer countries that had been exposed to more intense warming.

Link Between Climate Change And Parkinson's Disease Indicators

Table A (reported in Appendix) lists, for the 185 countries reported by Dorsey et al. (2018) for which temperature data were available, the two climate indices (see Methods for their definition) and the 1990-2016 variations of the PD patients' epidemiological data relative to deaths, prevalence and DALYs numbers.

In terms of the 1990-2016 warming index, values vary between -0.3°C and 1.8°C , with a median of 0.7°C , while in terms of 2016 average temperatures (T2016), values vary between -15.9°C and 29.1°C , with a median of 23.2°C (Tab. 1). It is worth noting that warming is, in general, more pronounced in colder countries, as can be seen by the scatter diagram of the warming index versus T2016 (Fig.1).

Tab. 1 Distribution of warming indices and T2016. Minimum and maximum, 25th and 75th percentile, and median values of the distribution of the 1990-2016 warming indices and the T2016 of the 185 countries.

	1990-2016 Warming Index	T2016
Min	-0.3	-15.9
25 th	0.4	11.8
Median	0.7	23.2
75 th	1.2	26.3
Max	1.8	29.1

By considering the 1990-2016 warming index and the T2016, the 185 countries (App. A) have been grouped in 4 categories (Fig. 1):

- the high-temperature and high-warming (HT-HW) category, which includes the 25 ones with above median climate indices (the ones represented by the dots in the top-right quadrant of the scatter plot shown in Fig. 1);

- the high-temperature and low-warming (HT-LW) category, which includes 68 countries (the ones in the bottom-right quadrant of Fig. 1);

- the low-temperature and high-warming (LT-HW category, which includes 68 countries (the ones in the top-left quadrant of Fig. 1));
- the low-temperature and low-warming (LT-LW category, which includes 24 countries (the ones in the bottom-left quadrant of Fig. 1)).

To assess whether there is any relationship between climate warming and variations in the PD indices, we have computed the correlation between the 1990-2016 variations of the PD indices and the 1990-2016 climate warming index firstly for all countries, and then for the countries grouped in the 4 categories defined above. Results (Tab. 2) indicate that the correlation is higher, and reaches 26%, for the countries in the HT-HW category, while for the other countries the correlation is close to zero.

Tab. 2 Correlation coefficients distribution. Correlation coefficients between the 1990-2016 variations of the PD indices and the climate warming index, computed for PD patients' deaths, prevalence and DALYs for countries in the 4 categories (HT-HW, HT-LW, LT-HW and LT-LW) and for all countries.

Category	Correlation of the 1990-2016 variation of the PD index and the climate warming index		
	Deaths	Prevalence	DALYs
HT-HW	26.3%	25.6%	26.1%
HT-LW	2.0%	1.6%	0.4%
LT-HW	0.5%	0.8%	0.4%
LT-LW	0.1%	4.1%	0.1%
ALL countries	0.2%	0.8%	0.02%

Tab. 3 T-test percent. T-test computed between the HT-HW distribution and the distributions of the HT-LW, LT-HW and LT-LW, for PD patients' deaths, prevalence and DALYs.

T-TEST	HT-HW		
	Deaths	Prevalence	DALYs
HT-LW	0.4%	0.0%	0.1%
LT-HW	0.2%	2.0%	0.5%
LT-LW	4.8%	0.1%	1.6%

Figure 2 shows, for the HT-HW countries, the scatter plot of the 1990-2016 variations of the PD indices as a function of the warming index. Note the positive slope for all 3 PD indices, indicating that for countries characterized by a warm climate (warmer T2016 than the median of all 185 countries), the variations of PD indices are higher in the countries that have been subjected to the largest warming. Although the

correlation is small, around 26%, this result can be seen as an indication that environmental factors linked to climate change could have contributed to the largest variations.

As a further indication that, for the HT-HW countries, climate warming played a role in inducing an increase in the PD patients' epidemiological indices, Fig. 3 shows the median, 25th and 75th percentile of the distribution of the PD indices for the 4 categories. Note that, for all 3 PD indices, there is a clear difference between the HT-HW distribution, and the distributions of the other 3 categories. To assess how the similarity between the distributions of the 1990-2016 variations of the PD indices of the HT-HW countries, and the distributions of the other categories, the t-test has been computed. Results (Tab. 3) show that for all indices but deaths, the probability that the two distributions are similar is less than 2%, while for deaths it is 4.8%. In other words, at the 95% level we can reject the null hypothesis that there is not any difference between the distribution of the HT-HW countries, and the countries of the other 3 categories.

Methods

Epidemiological and climate data. Epidemiological data analysed (prevalence, deaths and DALYs) were derived from Dorsey et al (2018). Climate data were extracted from the World Bank Climate Change Data Portal (freely available from The World Bank web site: <https://data.worldbank.org/indicator>), which includes, for almost all countries of the world, the monthly average temperature from 1990 to 2016.

Climate indices. Two climate indices have been defined, and computed:

- The 2016 average temperature (T2016), computed as the annual mean 2-meter temperature.
- The 1990-2016 warming index, which is a function of the slope of the linear regression curve that fitted the monthly 2-meter temperature data from January 1990 to December 2016; more precisely, it has been defined as the 26-year warming, between 1990 and 2016, computed from the linear-fitted curve (we used this index, rather than the difference between the annual average temperatures of 2016 and 1990, to represent in a more correct way the 26-year warming, and avoid the impact of annual variations).

According to these indices, countries with warmer climate have a higher value of T2016, and countries more affected by climate change have a higher warming index.

Countries selection. All the 194 countries listed in Dorsey et al (2018) have been considered. For 185 of them, monthly average temperature data were extracted from the World Bank Climate Change Data Portal, and their climate indices have been computed. They have been clustered in four categories, by comparing their indices (warming and T2016) against the sample median.

Statistical analysis and tests. Standard statistical methods have been applied to identify median and quartiles (see, e.g., Wilks 2019), compute correlations and assess results' robustness (t-test values).

Discussion

The average age of the world population is increasing and with it all the diseases linked to aging. Environmental temperatures are increasing too, and therefore we are wondering more and more if there is a relationship between these events. In our work we, indeed, have found evidence of a link between climate change-induced temperature variations and PD patients' epidemiological data between 1990 and 2016. We show that for the countries characterized by warmer than average climate and by more intense warming between 1990 and 2016, there is a significant correlation between the warming index and the variations in the PD patients' epidemiological indices.

Considering the HT-HW countries, we find both developing countries (e.g., Ethiopia, Somalia) and others with a high standard of living limited to the wealthiest social classes (e.g., Guatemala, Venezuela, Brazil, Kuwait, Oman), in which the majority of the population can be directly exposed to the effects of environmental heating. An average warming of few degrees implies that there is a higher probability of more intense and longer heat waves. So, if we consider the observed global average warming of about 1.2 degrees (from the pre-industrial level) in many countries, this has implied more frequent, longer and more intense heat waves that can have major impact on human health. For example, it is worth reminding the impact that the extended heat wave that hit Europe in the summer of 2003 had on mortality rates. For the future, a further warming of another 1-2 degrees could mean more frequent summer-2003-type of summers, and thus more heat-induced deaths.

From our findings, it appears that chronic exposure to higher temperatures in environments that are already warmer than others correlate with the onset of neurodegenerative events of clinical relevance. It can be hypothesized that populations already exposed to higher temperatures have a thermoregulation system more prone to develop neuroinflammatory events (Bongioanni et al., 2021). A plethora of both molecular and metabolic features related to organ homeostasis (e.g., hypothalamus control, hormonal networks, heat shock proteins) is activated in living endothermic organisms that can compensate for temperature changes. However, some of those features can be altered during aging, diseases or excessive heat exposure leading to a greater predisposition to aggravation of neurodegenerative disease. Moreover, when the external temperature varies by even one degree due to enhanced global warming, an acclimatization process begins (Lim, 2020) causing, if prolonged, the activation of biochemical pathways (such as oxidative stress and excitotoxicity) ultimately linked to neurodegeneration (Zammit et al., 2021). The main molecular pathways altered by temperature, affecting neuronal health and potentially causing the onset of neurodegenerative diseases (Lee et al., 2015; Chauhan et al., 2017), have been reported and discussed in a recent review by Bongioanni et al. (2021). All effects are amplified particularly in elderly people, whose thermoregulation is compromised.

Our results are particularly important since the HT-HW countries are home of about 912 million people, which is about 12% of the world population (based on 2020 data). With the climate-induced warming projected to double in the next decades (IPCC 2014) unless a drastic reduction in greenhouse gas

emissions is achieved, these and the other countries that will experience warmer climates could be affected by even larger increases than the one documented in this work.

Our findings deserve to be confirmed by further studies using possibly larger diachronic databases relating to both climatic variations and epidemiological parameters of PD patients and other subjects suffering from neurodegenerative diseases. Work along these lines should be encouraged.

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Figures

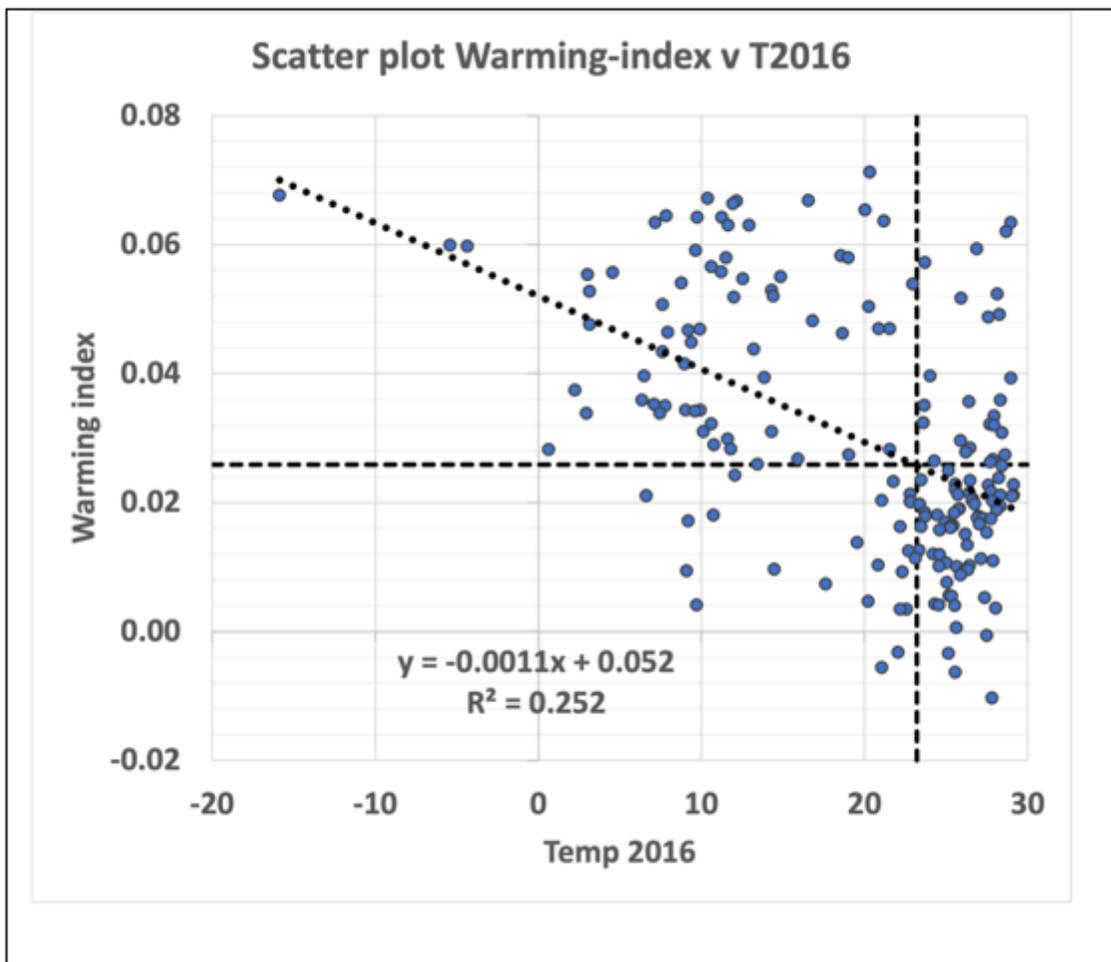


Figure 1

Graphical distribution of countries by warming index. Scatter plot of the 1990-2016 warming index versus the T2016, computed from 2-meter temperature values. Each symbol represents one of the 185 analysed countries (see Table in Appendix A). The horizontal and vertical lines divide the countries in the 4 categories high/low temperature, high/low warming. The dotted inclined line shows the linear fit of the warming index with respect to T2016 ($y = -0.0011x + 0.052$).

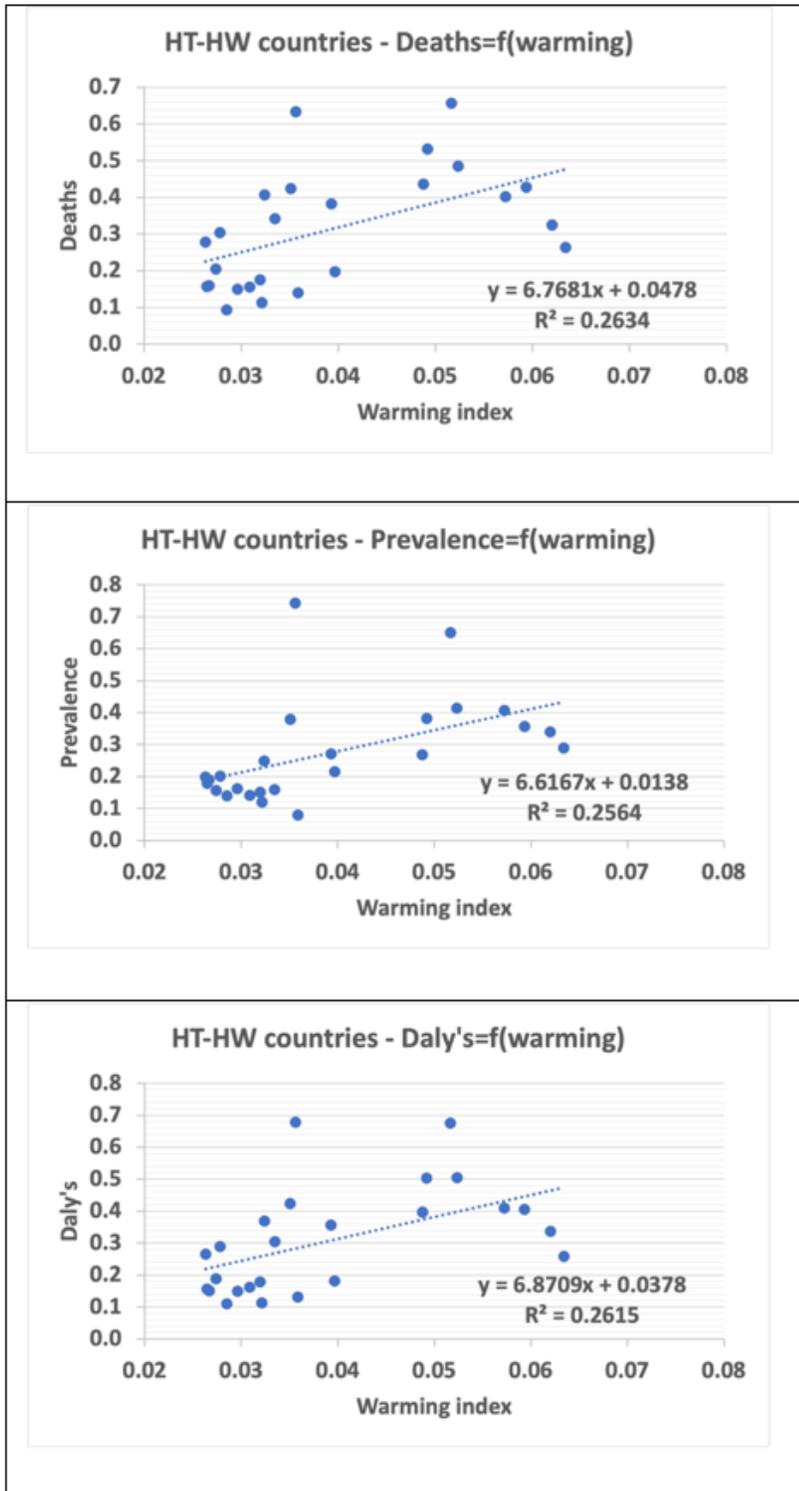


Figure 2

Warming index and DALYs correlation. HT-HW countries relationship between 1990-2016 variations of the PD indices and climate warming, for PD patients' deaths (top panel), prevalence (middle panel) and DALYs (bottom panel). Each dot represents one of the 25 HT-HW countries.

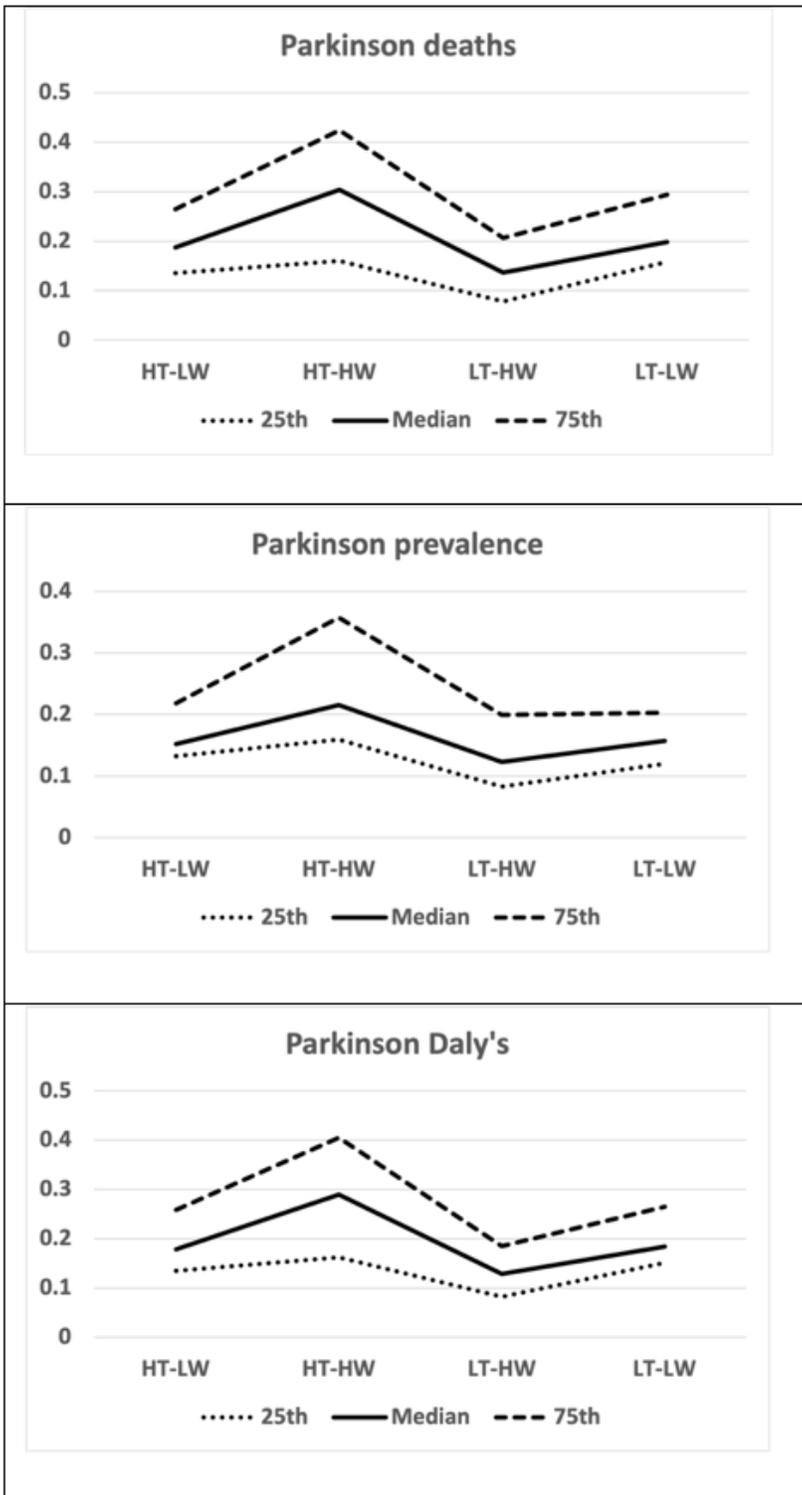


Figure 3

Warming index and epidemiological data correlation. The top panel refers to the 1990-2016 variations of the PD patients' deaths: for each of the 4 categories of countries HT-LW; HT-HW, LT-HW; LT-LW the 25th

percentile (dotted line), the median (solid curve) and the 75th percentile (dashed line). The middle panel refers to the 1990-2016 variations of PD prevalence. The bottom panel refers to the 1990-2016 variations of PD patients' DALYs.

Supplementary Files

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