Long-term association between the intensity of cosmic rays and mortality rates in the city of Sao Paulo

Environmental Research Letters

LETTER

Long-term association between the intensity of cosmic rays and mortality rates in the city of Sao Paulo

C L Z Vieira[1,2,7], E Janot-Pacheco[3], C Lage[5], A Pacini[4], P Koutrakis[2], P R Cury[6], H Shaodan[2], L A Pereira[1] and P H N Saldiva[1]

[1] Experimental Air Pollution Laboratory, Department of Pathology, Medical School, University of Sao Paulo, Sao Paulo, Brazil
[2] Department of Environmental Health, Harvard School of Public Health, Boston, MA, United States of America
[3] Institute of Astronomy, Geophysics and Atmospheric Sciences, University of Sao Paulo, Sao Paulo, Brazil
[4] Applied Physics Laboratory, John Hopkins University, Laurel, MD, United States of America
[5] Instituto de Biofisica Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[6] Department of Periodontology, Federal University of Bahia, Salvador, Brazil
[7] Author to whom any correspondence should be addressed.

E-mail: cazilli@hsph.harvard.edu

OPEN ACCESS

RECEIVED
22 February 2017

REVISED
29 November 2017

ACCEPTED FOR PUBLICATION
18 December 2017

PUBLISHED
1 February 2018

Keywords: solar cycles, galactic cosmic radiation, temperature, epidemiology, risk factor

Supplementary material for this article is available online

Abstract

Human beings are constantly exposed to many kinds of environmental agents which affect their health and lifespan. Galactic cosmic rays (GCRs) are the main source of ionizing radiation in the lower troposphere, in which secondary products can penetrate the ground and underground layers. GCRs affect the physical–chemical properties of the terrestrial atmosphere, as well as the biosphere. GCRs are modulated by solar activity and latitudinal geomagnetic field distribution. In our ecological/populational retrospective study, we analyzed the correlation between the annual flux of local secondary GCR-induced ionization (CRII) and mortality rates in the city of Sao Paulo, Brazil, between 1951–2012. The multivariate linear regression analyses adjusted by demographic and weather parameters showed that CRII are significantly correlated with total mortality, infectious disease mortality, maternal mortality, and perinatal mortality rates ($p < 0.001$). The underlying mechanisms are still unclear. Further cross-sectional and experimental cohort studies are necessary to understand the biophysical mechanisms of the association found here.

Introduction

The Earth's atmosphere is constantly bombarded by a variety of sources of extra-terrestrial ionizing radiation, such as galactic cosmic rays (GCRs) (Calisto *et al* 2011, Usoskin and Kovaltsov 2006, Usoskin *et al* 2011, Usoskin *et al* 2009). Observations have shown that many large short-term increases in the GCR flux from nearby supernovae are strongly associated with the cooling of the Earth's climate and biodiversity crises over the past million years (Svensmark 2012). It is well known that chronic exposure to GCRs at high altitudes is strongly associated with cancer, e.g. leukemia in aircraft crew and astronauts (Swenberg *et al* 1991). Additionally, there is evidence connecting exposure to secondary background GCRs with increased occurrence of cancer, myocardial infarction, congenital anomalies, and mortality rates (Juckett 2007, Spycher *et al* 2015, Juckett 2009, Stoupel *et al* 2011).

GCRs consist of charged subatomic particles (mostly protons, ~10% He nuclei, ~1% electrons, and ~1% other elements) traveling near the speed of light, with energies from about 1 MeV ($1\,\text{MeV} = 1.6 \times 10^{-13}$ J) up to 5×10^{13} MeV. They mainly originate from supernovae remnants in the Solar System neighborhood (Usoskin *et al* 2009). The intensity of GCRs is modulated by the magnetized solar wind plasma and by the Earth's magnetic field according to an 11 year solar activity cycle (Usoskin *et al* 2009). In solar maxima epochs (where there are the highest numbers of sunspots), GCR penetration becomes lower in the Earth's atmosphere, and higher during solar minima. The collisions between primary GCRs and atmospheric gas molecules result in a cascade of chemical and physical reactions producing

secondary cosmic rays, which penetrate the Earth's surface and underground layers (Calisto *et al* 2011, Usoskin and Kovaltsov 2006, Usoskin *et al* 2009, Li and Beacom 2015). All of these processes result in atmospheric air ionization, which has been associated with atmospheric electricity, cloudiness, and climate, all affecting human health (Kirkby *et al* 2011, Kirkby 2007).

The impact of CRII—as a type of low-level intensity of high-energy ionizing radiation—on human health at ground level is still unknown. Therefore, the aim of this study was to investigate the association between CRII and mortality rates in the city of Sao Paulo, Brazil from 1951–2012. The association between mortality rates and numbers of sunspots, local temperature and relative humidity was also analyzed. Located at nearly 770 m (2522 ft) above sea level, the city of Sao Paulo (23°32'S, 46°38'W) is the largest city in Brazil. Sao Paulo ranks amongst the top ten most populous urban cities in the world and has the second highest per capita income in Brazil according to the National Institute of Geography and Statistics of Brazil (IBGE). The population of the city of Sao Paulo was estimated at 2198 096 in 1950, and reached 11 967 825 inhabitants in 2015 (IBGE).

Data and methods

Mortality data

Death certificates [number of deaths, both genders, all standardized age ranges from ≤1 to ≥75 years old (≤1; 0–4; 5–9; 10–14; 15–19; 20–24; 25–29; 30–34; 35–39; 40–44; 45–49; 50–54; 55–59; 60–64; 65–69; 70–74 and ≥75 years old)] and the census tract of residence at the time of death for each individual in the city of Sao Paulo from 1951–2012 were obtained from the State System of Statistical Data (SEADE) (supplementary table 1 available at stacks.iop.org/ERL/13/024009/mmedia). We considered causes of death from the codes A00 through T98 according to the International Statistical Classification of Diseases, 10th Revision (ICD 10th) (supplementary table 1). For our analyses, we calculated mortality rates as the total number of deaths by cause of mortality per total number of inhabitants. Mortality rates were considered response variable in the outputs.

Environmental assessment data

To analyze the exposure to secondary GCRs at ground level, we calculated the sum of paired ions cm^{-3} sec^{-1} produced by primary and secondary GCRs in atmospheric reactions based on the CRII model described by Usoskin and Kovaltsov (2006) (figure 1). Roughly, 1500 paired ions cm^{-3} sec^{-1} is equivalent to 0.2 mSv yearly. Data on the number of sunspots (ISSN, or Zurich number) was acquired from the Oulu Cosmic Ray Station database of the University of Oulu (Usoskin and Kovaltsov 2006). Daily temperature averages (°C), and relative humidity (%RH) were provided by the Institute of Astronomy, Geophysics and Atmospheric Sciences of University of Sao Paulo (IAG-USP) since 1950. Monthly and daily values obtained were subsequently converted to annual means. To analyze the mortality rates during periods of solar cycle minima and maxima, data on the number of sunspots were categorized as 0 when the number was <80 ISSN (periods of solar minima ± 6 years) and 1 when the value was >80 ISSN (periods of solar maxima ± 5 years). The variables CRII average, number of sunspots, temperature, relative humidity, demographic parameters (age and gender), and year were considered as explanatory variables.

Statistical analyses

Statistical analyses started by performing calculations with obtained data, such as means, medians, percentiles and standard deviations for all variables following a normal distribution. Pearson and Spearman rank analyses were done to check the correlation between the independent variables (CRII, number of sunspots, local temperature, %RH, year) and mortality rates (considering 'all ages' or 'age ranges'). *T*-test analyses were performed to compare the mortality rate trends during epochs of solar maxima and minima (considering 'number of sunspots' as the categorized variable) for both genders and all standardized age ranges. For multivariate linear regression analyses, the final models were fitted using a stepwise addition of variables to select significant explanatory variables for each cause of mortality rate, which was examined first and retained throughout the subsequent scrutiny. Multiple linear regression analysis was applied to estimate the correlation between annual mortality rates and the mean CRII, local temperature and RH (when selected in the stepwise regression). The models were adjusted by age, gender and year with a 95% confidence interval (CI). All analyses were conducted with the statistical software SAS 9.8. Predicted probabilities and 95% CIs were used to visualize mortality trajectories. The level for significance was set at $p \leq 0.05$.

Results

In this study, all variables fitted a normal distribution. From 1951–2012, all causes of mortality (mean 52 873 deaths) were distributed among different categories in which 3604 deaths were from infectious diseases, 7524 from neoplasms, 15 918 from circulatory diseases, 6023 from respiratory diseases, 2 975 from perinatal complications, and 5 750 from external causes and others (supplementary table 2). Plots relating average solar activity and mortality rates are shown in figure 2. In the correlation analyses, we observed that CRII and number of sunspots were not significantly correlated with mortality rates. Colder temperatures were strongly correlated with total mortality, maternal

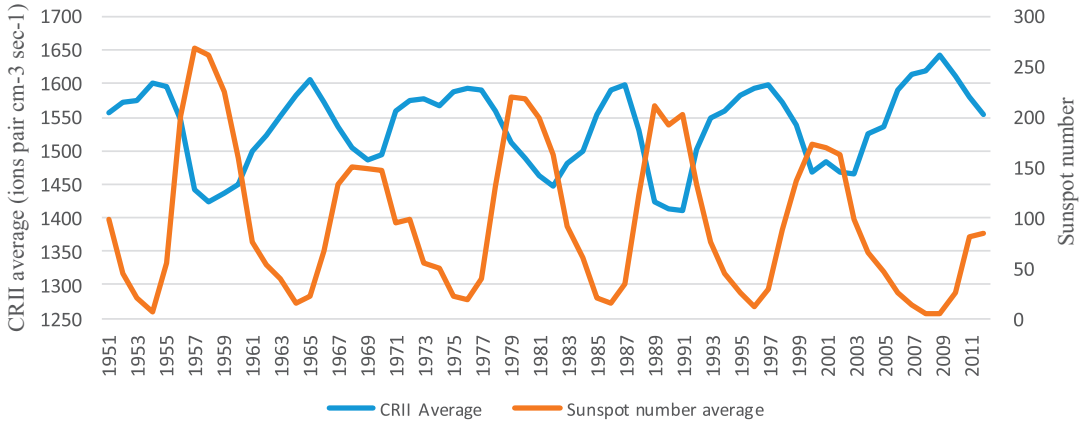

Figure 1. Distribution of CRII and number of sunspots in Sao Paulo city from 1951–2012.

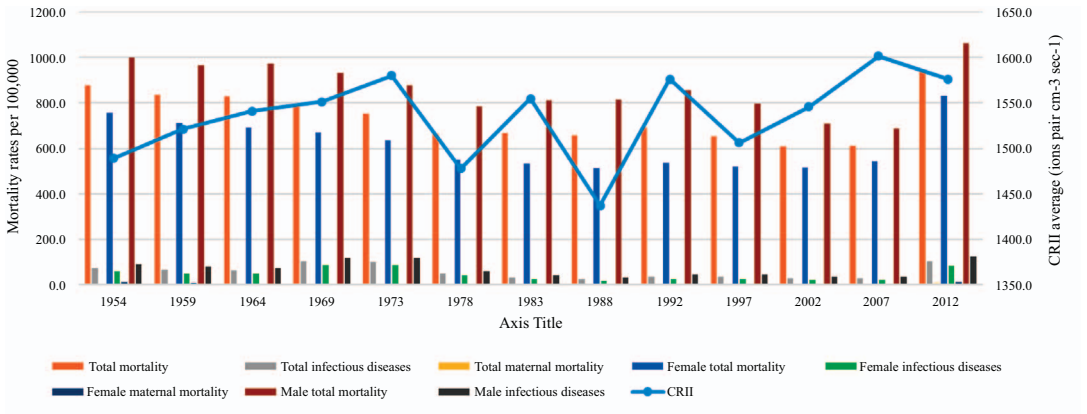

Figure 2. CRII and mortality rates fluctuations in Sao Paulo city from 1951–2012.

mortality, and perinatal and congenital mortality rates ($r > 0.7$, $p < 0.001$), and were weakly correlated with other mortality rates ($r < 0.5$, $p < 0.05$). To compare the mean mortality rates with standardized age ranges during periods of solar minima and maxima, we performed a *t*-test analysis. During epochs of solar minima (when CRII is high), there was a significant increase in the mean mortality rates ($p < 0.05$) for the diseases listed below (table 1). The correlation between CRII and all causes of death in women were significantly higher than in men and children, excluding perinatal mortality rates.

In the multiple linear regression analyses adjusted by age, gender and year (table 2), CRII were strongly and positively correlated with total mortality ($R^2 = 0.9$, $p < 0.0001$), maternal mortality ($R^2 = 0.8$, $p < .0001$), perinatal mortality ($R^2 = 0.9$, $p = 0.001$), and infectious disease mortality ($R^2 = 0.6$, $p < 0.0001$) rates, and negatively correlated with congenital mortality rates ($R^2 = 0.9$, $p < 0.0001$) (table 2). No or weak correlations were found between CRII other mortality rates analyzed in the present study (supplementary table 2). Data on the number of sunspots have no or negative correlation with mortality rates in the linear regression analysis. Sunspot activity was considered a surrogate for CRII fluctuation, since these two are anti-correlated (figure 1), which is in agreement with the literature, and not correlated with temperature or %RH ($p > 0.05$) (data not shown).

Differences between the results found in the *t*-test and linear regression analyses can be justified as follows: in the regression analysis mortality rates could not be split according to standardized ages, as the lower coefficients would dismiss the evidence raised by a more global analysis. Hitherto, stronger associations between CRII and mortality rates for some diseases were observed when the regression analysis was performed under the 'all ages together' parameter. Thus, according to the *t*-test results, mortality rates for each disease age range along the surveyed 11 year solar cycles revealed that periods of raised CRII were significantly associated with higher mortality rates for most of the age ranges analyzed.

Discussion

Human beings are continuously exposed to many kinds of environmental agents, e.g. radiation and air pollution, which can affect their behavior, health outcomes

Table 1. Significant variance between periods of solar minima and solar maxima by standardized age ranges in Sao Paulo city[a].

Cause of deaths	All standardized age ranges**	Mean		Standard deviation (95% CI)		*p*-value
		Solar minimum*	Solar maximum*	Solar minimum*	Solar maximum*	
Infectious diseases	35–39	**4.4**	3.1	2.4	1.9	0.02
	40–44	**4.4**	2.9	2.7	1.6	0.01
	45–49	**4.1**	2.7	2.8	1.4	0.01
	50–54	**3.7**	2.4	2.5	1.1	0.01
	55–59	**3.3**	2.1	2.4	0.8	0.01
	60–64	**3.0**	1.8	2.2	0.64	0.007
	65–69	**2.6**	1.5	0.4	0.04	0.008
	70–74	**2.4**	1.2	2.5	0.3	0.01
	≥75	**6.5**	2.3	8.6	0.9	0.01
Neoplasms	10–14	**0.8**	0.6	0.4	0.2	0.02
	15–19	**1.2**	0.8	0.5	0.3	0.003
	20–24	**1.4**	1.0	0.72	0.4	0.01
	25–29	**2.0**	1.4	1.1	0.5	0.005
	30–34	**3.0**	2.0	1.5	0.66	0.004
	35–39	**4.3**	3.1	2.1	1.0	0.007
	40–44	**7.1**	4.0	4.0	1.3	0.007
	45–49	**10.8**	7.1	7.1	1.3	0.008
	55–59	**18.7**	11.3	14	1.5	0.006
	60–64	**20.7**	12.7	15.4	1.2	0.005
	65–69	**20.9**	12.7	16.3	1.3	0.008
	70–74	**20.5**	11.7	18.0	2.1	0.01
	≥75	**41.6**	19.1	46.9	8.0	0.01
Blood diseases	5–9	**0.12**	0.08	0.08	0.05	0.01
	10–14	**0.09**	0.06	0.05	0.03	0.002
	15–19	**0.12**	0.08	0.08	0.06	0.03
	20–24	**0.17**	0.1	0.09	0.04	0.0003
	25–29	**0.1**	0.09	0.08	0.05	0.0009
	30–34	**0.14**	0.08	0.09	0.04	0.0007
	35–39	**0.1**	0.08	0.1	0.03	0.004
	40–44	**0.16**	0.09	0.15	0.05	0.009
	45–49	**0.2**	0.1	0.1	0.04	0.01
	50–54	**0.24**	0.11	0.25	0.05	0.008
	55–59	**0.2**	0.1	0.2	0.05	0.009
	60–64	**0.26**	0.12	0.25	0.06	0.006
	65–69	**0.2**	0.1	0.2	0.05	0.007
	70–74	**0.34**	0.13	0.37	0.07	0.003
	≥75	**1.1**	0.3	1.5	0.2	0.01
Endocrine diseases	25–29	**13.7**	10.3	7.5	2.9	0.02
	30–34	**11.6**	8.1	6.2	1.9	0.005
	35–39	**9.7**	6.6	5.7	1.5	0.006
	40–44	**8.3**	5.4	5.5	1.4	0.008
	45–49	**6.8**	4.4	5.0	1.1	0.01
	50–54	**5.8**	3.5	4.4	1.1	0.008
	55–59	**4.6**	2.8	3.6	0.9	0.01
	60–64	**3.8**	2.5	2.8	1.2	0.01
	65–69	**3.2**	2.1	2.5	1.1	0.02
	70–74	**2.9**	1.9	2.5	1.2	0.04
	≥75	**8.6**	3.8	10.5	2.9	0.01
Nervous system diseases	**10–14**	**0.5**	0.4	0.3	0.2	0.04
	15–19	**0.6**	0.4	0.4	0.3	0.003
	20–24	**0.74**	0.52	0.36	0.3	0.01
	25–29	**1.0**	0.5	0.43	0.4	0.03
	30–34	**1.0**	0.7	0.6	0.53	**0.05**
	35–39	**1.2**	0.7	0.8	0.7	0.03
	40–44	**1.6**	1.0	1.3	1.1	**0.05**
	45–49	**2.1**	1.3	1.9	1.6	**0.07**
	50–54	**2.6**	1.6	2.6	1.3	**0.11**
	55–59	**3.1**	1.9	3.2	2.8	**0.12**
	60–64	**3.8**	2.3	4.1	3.7	**0.16**
	65–69	**4.2**	2.4	4.6	3.6	**0.08**
	70–74	**4.5**	2.5	4.4	3.7	**0.05**
	≥75	**15.2**	5.4	14.2	7.2	0.001
Genitourinary diseases	55–59	**1.5**	0.97	1.1	0.4	0.01
	60–64	**1.7**	1.0	1.4	0.43	0.01
	65–69	**2.1**	1.2	1.7	0.4	0.007
	70–74	**2.5**	1.2	2.4	0.36	0.003
	≥75	**10.2**	3.5	13.8	1.8	0.01

[a] *t*-test analysis; * rates per 100 000; ** years old.

Table 1. *Continued.*

Cause of deaths	All standardized age ranges**	Mean		Standard deviation (95% CI)		*p*-value
		Solar minimum*	Solar maximum*	Solar minimum*	Solar maximum*	
Digestive diseases	25–29	**1.2**	0.9	0.46	0.43	0.007
	30–34	**2.1**	1.5	0.72	0.56	0.005
	35–39	**3.1**	2.2	1.3	0.5	0.001
	40–44	**4.3**	2.8	2.4	0.5	0.0009
	45–49	**5.3**	3.1	3.6	0.5	0.002
	50–54	**5.9**	3.2	4.5	0.6	0.002
	55–59	**5.8**	3.2	4.5	0.6	0.003
	60–64	**5.5**	3.1	4.2	0.67	0.002
	65–69	**5.3**	2.8	4.3	0.5	0.003
	70–74	**5.1**	2.5	4.6	0.61	0.004
	≥75	**13.1**	5.3	15.3	2.5	0.008
Circulatory diseases	35–39	**6.9**	5.7	1.7	1.6	0.004
	40–44	**10.7**	8.3	3.8	1.7	0.002
	45–49	**15.2**	11.6	7.2	1.8	0.009
	50–54	**21.5**	15.4	11.5	2.6	0.005
	55–59	**26.3**	18.9	15	2.7	0.01
	60–64	**32.3**	23	17.2	3.6	0.005
	65–69	**36.6**	26.1	20.7	4.0	0.009
	70–74	**40.6**	28.1	25.6	4.8	0.01
	≥75	**125**	74.1	105	13.9	0.01
Respiratory diseases	10–14	**0.5**	0.4	0.1	0.2	0.03
	15–19	**1.0**	0.6	0.20	0.18	0.002
	25–29	**1.5**	1.2	0.4	0.4	0.01
	30–34	**2.0**	1.6	0.53	0.5	0.01
	35–39	**2.4**	1.9	0.6	0.4	0.001
	40–44	**2.8**	2.1	1.1	0.43	0.002
	45–49	3.4	2.2	2.1	0.2	0.003
	50–54	**4.2**	2.6	3.2	0.4	0.006
	55–59	**5.2**	3.0	4.4	0.7	0.01
	60–64	**6.6**	3.7	5.6	0.99	0.007
	65–69	**8.4**	4.6	7.6	1.6	0.01
	70–74	**10.8**	5.5	10.9	2.2	0.01
	≥75	**47.6**	19.6	59.4	12.3	0.01
External causes	25–29	**13.7**	10.3	7.5	2.9	0.02
	30–34	**11.6**	8.1	6.2	1.9	0.005
	35–39	**9.7**	6.6	5.7	1.5	0.006
	40–44	**8.3**	5.4	5.5	1.4	0.008
	45–49	**6.8**	4.4	5.0	1.1	0.01
	50–54	**5.8**	3.5	4.4	1.1	0.008
	55–59	**4.6**	2.8	3.6	0.9	0.01
	60–64	**3.8**	2.5	2.8	1.2	0.01
	65–69	**3.2**	2.1	2.5	1.1	0.02
	70–74	**2.9**	1.9	2.5	1.2	0.04
	≥75	**8.6**	3.8	10.5	2.9	0.01

Table 2. Multiple linear regression analysis of the correlation between CRII exposure and mortality by specific diseases in the population of Sao Paulo city from 1951–2012.

Mortality rates	Independent variable	*β*-coefficient	95% confidence limits		*p*-value
Total mortality ($R^2 = 0.9$)	**Intercept**	0.10954	0.10778	0.1113	<.0001
	CRII*	2.81	2.61	3.02	<.0001
	Temperature**	−74.0	−102.25	−45.74	<.0001
Infectious diseases ($R^2 = 0.6$)	**Intercept**	0.02377	0.02283	0.02471	<.0001
	CRII*	1.02	0.9	1.13	<.0001
	Temperature**	1.63	−6.4	9.65	0.691
Perinatal period ($R^2 = 0.9$)	**Intercept**	0.02979	0.02923	0.03035	<.0001
	CRII*	0.03	0.01	0.05	0.001
	Temperature**	−13.99	−22.98	−5.0	0.0023
Maternal mortality ($R^2 = 0.8$)	**Intercept**	0.00132	0.00127	0.00136	<.0001
	CRII*	0.03	0.02	0.03	<.0001
	Temperature	−0.00001	−0.5	0.5	1
Congenital diseases ($R^2 = 0.9$)	**Intercept**	0.00508	0.00499	0.00517	<.0001
	CRII*	−0.02	−0.03	−0.015	<.0001
	Temperature**	−0.3	−1.34	0.7	0.5135
	RH***	0.9	0.6	1.07	<.0001

* paired ions cm^{-3} sec^{-1}; ** °C; ***RH: relative humidity, CRII, temperature and RH values represent rates per 100 000.

and lifespan. Historically, GCRs have posed a threat during Earth's mass extinctions where they are accompanied by high rates of mutations over geological time scales (Clark *et al* 1977, Svensmark 1998, Svensmark 2012). Except during catastrophic geological periods, regular 11 year and 22 year solar cycles modulate the penetration of GCRs, which does not usually vary much from one cycle to another. Nevertheless, the health impact of long-term exposure to local GCRs during regular solar cycles awaits clarification, while it may have been silently driving genetic evolution throughout human history on Earth.

In this ecological/populational retrospective study, strong correlations between CRII and total mortality, infectious diseases, maternal mortality, and perinatal mortality rates were observed in the city of Sao Paulo. Annually, ~336 total deaths may be attributed to CRII exposure in the city of Sao Paulo. Low temperatures were correlated with total mortality and perinatal mortality rates.

Among all secondary sources of GCRs comprised in CRII, muons and neutrons dominate the GCR flux at background and underground terrestrial layers (Li and Beacom 2015). The direct effects of muons on living beings are difficult to measure (Atri and Melott 2011), but it is known that muons and neutrons can penetrate, and even cross, biological structures, transferring their energy into the surrounding media (Atri and Melott 2011, Sanche 2005). In these processes, new secondary subatomic particles are produced, targeting other atoms and molecules resulting in ionization trails and, occasionally, mutations according to their energies (Atri and Melott 2011). Muon-induced ionization can affect cellular functions by directly inducing mutagenic DNA damage, but more likely by indirectly generating free radical species, such as the hydroxyl radical $OH^{\bullet}$ or the oxygen radicals $O_2^{\bullet}/HO_2^{\bullet}$, which can promptly target DNA causing mutagenic-prone damage, and also modifying gene expression and transcriptional networks (Hitschke *et al* 1994).

Continuous exposure to background CR neutrons of a lower intensity has been linked to the increase of individual predispositions to cancer and premature mortality due to GCR-induced congenital disorders (Juckett 2009), cardiac arrhythmias and myocardial infarction (Stoupel *et al* 2006), and total number of deaths (Stoupel *et al* 2011). Petropoulos *et al* (2006) also described a positive correlation between variations in CR levels and heart rate variability in patients with no cardiac symptoms and hospital admissions during 2002–2005 in Athens, Greece. In the present study, no positive correlation between CRII and mortality by circulatory diseases and congenital mortality rates was found in the linear regression analyses.

Aside from having a strong association with total mortality, CRII appears to have strongly impacted mortality related to perinatal mortality (table 2) in Sao Paulo in the 1951–2012 period (figure 2). The biological plausibility of our results may find support in the expected accumulative effects of CRII on susceptible individuals, genetically characterized by their high-radiosensitivity as described by Watson *et al* (1997). Both direct and indirect effects of radiation trigger a series of biochemical signals with associated cascades of molecular events that may repair the damage or, if permanent physiological changes remain, lead to cellular death (Azzam *et al* 2012).

Juckett (2009) observed that human longevity and mortality by cancer exhibited regular and highly synchronous variations with the background fluxes of CR neutrons. He hypothesized that ancestral generations of a newborn child could have accumulated CR neutron-induced epigenetic markers, carrying an inappropriate epigenetic imprint characterized by a higher individual predisposition to cancer, when exposed to other environmental agents that cause genetic mutations. Moreover, the fetal brain reaches its maximum vulnerability between the eighth to fifteenth week after fertilization when exposed to low-level ionizing radiation (Yamazaki and Schull 1990). Indeed, hemopoietic stem cells of mammals are highly sensitive to exposure to low-level ionizing radiation, which induces cellular damage that particularly affects the hemopoietic cell renewal systems, impairing immunoinflammatory activity and other physiological functions (Fliedner *et al* 2012).

Genetic mutations may be also induced by CRII in microorganisms spread out in the environment, temporarily re-introducing 'new' pathogens in the population and causing an increase in mortality from infectious diseases in periods of higher secondary GCR exposition. Host–parasite dynamics have a great potential to evolve and adapt to persistent unfavorable environmental conditions, reverting high mutation rates into an increase of their pathogenicity (Parikka *et al* 2012, Altizer *et al* 2006). One of the most interesting findings regarding this issue is that exposure to very low-dose ionizing radiation can prompt a survival response in bacterial cells when subsequently undergoing potentially lethal damage, acting as an adaptive dose. According to an original report by Parikka *et al* (2012), low dose radiation treatment is able to reactivate latent tuberculosis in infected zebrafish. Moreover, cycles of re/emergent infectious diseases have been linked to the evolution of the human immune system, improving the host defense and decreasing their susceptibility to new episodes of infectious diseases (Laayouni *et al* 2014). This mechanism could justify the normalization of infectious disease mortality rates in the subsequent regular peaks of CRII. Another hypothesis that may elucidate the association between GCRs and infectious disease mortality is the effects of GCRs on climatic variations, which may affect the incidence of infectious diseases. Climate change and infectious diseases have been strongly correlated, and these periods have been identified as the period when re/emergent microorganisms are reintroduced into societies (Altizer *et al* 2006). Moreover, the

association between CRII and mortality rates may also be reflecting other primary or secondary processes, such as those related to GCRs and atmospheric aerosol dynamics and cloudiness (Griffin 2007), GCRs and the global electrical circuit e.g. Schumann resonance (Rycroft *et al* 2000), and/or another unknown GCR mechanisms in the lower troposphere. The biosphere is indeed a proper region to convert GCRs into many active energy forms, such as electrical, chemical, mechanical, and thermal (Vernadsky 1998), which may affect human health through yet unknown mechanisms.

In contradiction to some studies that have described the association of high solar activity and human health in the literature (Palmer *et al* 2006, Hrushesky *et al* 2011), we observe no positive correlation between sunspot and mortality rates in our study. The cyclical and dynamic interaction of space-weather components driven by solar activity can affect human health and behavior, possibly by inducing unexpected episodes of higher oxidative stress, to which humans have to constantly adapt to live on Earth.

Study limitations

A strong correlation between CRII and mortality rates was statistically disclosed in a highly populated metropolitan city in this 52 year long ecologically-designed study. The interpretation of the exposure–outcome relationships regarding an environmental factor such as cosmic radiation may be limited by the possibility that another unpredicted agent could have exerted its effects on the observed outcomes. Nevertheless, it is relevant to remark that if ever such a cause exists, it follows the same 11 year cycle fluctuation pattern.

Another aspect of this study was that correlations between CRII and mortality rates were revealed when 'causes of death' were considered from the same ICD classification, instead of by types of diseases (according to the ICD 10th codes). Similar diseases have been grouped under the same ICD code, disregarding their few physiopathological differences and age of incidence. This might have overshadowed more significant correlations between CRII and mortality rates.

Conclusion

Our results are the first evidence in the literature that local secondary GCRs may affect mortality rates. The association between higher GCR fluxes with Earth's mass extinctions has been described in the literature, but the impact of continuous human exposure to low-level cosmic radiation background is still unclear. In addition, CR may be an agent that naturally induces genetic mutations in nature, promoting a slow evolution of all species on Earth, including microorganisms and humans.

Future survival analysis and experimental studies are fundamental to clarify how GCRs may affect human health, and these results will collaborate with preventive health models and programs to control unexpected increases of mortality rates in susceptible individuals due to higher peaks of GCRs on Earth.

Acknowledgments

We thank Professor Usoskin for valuable discussions regarding CRII and for providing all astrophysical data.
Author Disclosure Statement: No competing financial interests exist.
Financial Support: This project was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP process: 2013/15154-3).

ORCID iDs

C L Z Vieira https://orcid.org/0000-0002-8763-3331

References

Altizer S, Dobson A, Hosseini P, Hudson P, Pascual M and Rohani P 2006 Seasonality and the dynamics of infectious diseases *Ecol. Lett.* **9** 467–84
Atri D and Melott A L 2011 Biological implications of high-energy cosmic ray induced muon flux in the extragalactic shock model *Geophys. Res. Lett.* **38** 1–3
Azzam E I, Jay-Gerin J P and Pain D 2012 Ionizing radiation-induced metabolic oxidative stress and prolonged cell injury *Cancer Lett.* **327** 48–60
Calisto M, Usoskin I, Rozanov E and Peter T 2011 Influence of galactic cosmic rays on atmospheric composition and dynamics *Atmos. Chem. Phys.* **11** 4547–56
Clark D H, McCrea W H and Stephenson F R 1977 Frequency of nearby supernovae and climatic and biological catastrophes *Nature* **1977** 318
Fliedner T M, Graessle D H, Meineke V and Feinendegen L E 2012 Hemopoietic response to low dosage rates of ionizing radiation shows stem cell tolerance and adaptation *Dose-Response* **10** 644–63
Griffin D W 2007 Atmospheric movement of microorganisms in clouds of desert dust and implications for human health *Clin. Microbiol. Rev.* **20** 459
Hitschke K *et al* 1994 Inactivation of the Na, K-ATPase by radiation-induced free radicals evidence for a radical-chain mechanism *FEBS Lett.* **353** 297–300
Hrushesky W J, Sothern R B, Du-Quiton J, Quiton D F T, Rietveld W and Boon M E 2011 Sunspot dynamics is reflected in human physiology and pathophysiology *Astrobiology* **11** 93–103
Juckett D A 2007 Correlation of a 140 year global time signature in cancer mortality birth cohorts with galactic cosmic ray variation *Int. J. Astrobiol.* **6** 307–19
Juckett D 2009 A 17 year oscillation in cancer mortality birth cohorts on three continents—synchrony to cosmic ray modulations one generation earlier *Int. J. Biometeorol.* **53** 487–99
Kirkby J 2007 Cosmic rays and climate *Surv. Geophys.* **28** 333–75
Kirkby J *et al* 2011 Role of sulphuric acid, ammonia and galactic cosmic rays in atmospheric aerosol nucleation *Nature* **476** 429–33
Laayouni H *et al* 2014 Convergent evolution in European Rroma populations reveals pressure exerted by plague on Toll-like receptors *Proc. Natl Acad. Sci.* **111** 2668–73

Li S W and Beacom J F 2015 Spallation backgrounds in Super-Kamiokande are made in muon-induced showers *Phys. Rev.* D **91** 105005

Palmer S J, Rycroft M J and Cermack M 2006 Solar and geomagnetic activity, extremely low frequency magnetic and electric fields and human health at the Earth's surface *Surveys Geophys.* **27** 557–95

Parikka M *et al* 2012 *Mycobacterium marinum* causes a latent infection that can be reactivated by gamma irradiation in adult zebrafish *PLoS Pathog.* **8** e1002944

Petropoulos B, Mavromichalaki H, Papailiou M, Kelesidis K and Mertzanos G 2006 Similarity of subcardian and sharp variations of the cosmic ray intensity to heart variability *36th COSPAR Scientific Assembly (16–23 July, Beijing, China)*

Rycroft M J, Israelsson S and Price C 2000 The global atmospheric electric circuit, solar activity and climate change *J. Atmos. Sol. Terr. Phys.* **62** 1563–76

Sanche L 2005 Low energy electron-driven damage in biomolecules *Eur. Phys. J. D* **35** 367–90

Spycher B D, Lupatsch J E, Zwahlen M, Röösli M, Niggli F, Grotzer M A, Rischewski J, Egger M and Kuehni C E 2015 Background ionizing radiation and the risk of childhood cancer: a census-based nationwide cohort study *Environ. Health Perspect.* **123** 622–8

Stoupel E *et al* 2006 Are neutrons involved in in the pathogenesis of life threatening cardiac arrhythmias? *J. Basic Clin. Physiol. Pharmacol.* **17** 55–62

Stoupel E, Kalediene R, Petrauskiene J, Starkuviene S, Abramson E, Israelevich P and Sulkes J 2011 Twenty years study of solar, geomagnetic, cosmic ray activity links with monthly deaths number (n-850304) *J. Biomed. Sci. Eng.* **4** 426

Svensmark H 1998 Influence of cosmic rays on Earth's climate *Phys. Rev. Lett.* **81** 5027–30

Svensmark H 2012 Evidence of nearby supernovae affecting life on Earth *Mon. Not. R Astron. Soc.* **423** 1234–53

Swenberg C E, Horneck G and Stassinopoulos E G 1991 *Biological Effects and Physics of Solar and Galactic Cosmic Radiation Part A (Nato ASI Series)* (Algarve: Springer)

Usoskin I G and Kovaltsov G A 2006 Cosmic ray induced ionization in the atmosphere: full modeling and practical applications *J. Geophys. Res.* **111** D21206

Usoskin I G, Kovaltsov G A, Mironova I A, Tylka A J and Dietrich W F 2011 Ionization effect of solar particle GLE events in low and middle atmosphere *Atmos. Chem. Phys.* **11** 1979–88

Usoskin I G, Desorgher L, Velinov P, Storini M, Fluckiger E O, Butikofer R and Kovaltsov G A 2009 Ionization of the Earth's atmosphere by solar and galactic cosmic rays *Acta Geophys.* **57** 88–101

Yamazaki J N and Schull W J 1990 Perinatal loss and abnormalities among children of the atomic bomb. Nagasaki and Hiroshima revisited 1949–1989 *J. Am. Med. Assoc.* **264** 605–9

Vernadsky V I 1998 *The Biosphere* (New York: Springer)

Watson Ge, Lorimore S A, Clutton S M, Kadhim M A and Wright E G 1997 Genetic factors influencing alpha-particle-induced chromosomal instability *Int. J. Radiat. Biol.* **71** 497–503