BMJ Open  Do solar cycles influence giant cell arteritis and rheumatoid arthritis incidence?

Simon Wing,† Lisa G Rider,‡ Jay R Johnson,§ Federick W Miller,‡ Eric L Matteson,∥ Cynthia S Crowson,∥ Sherine E Gabriel

ABSTRACT

Objective: To examine the influence of solar cycle and geomagnetic effects on the incidence of giant cell arteritis (GCA) and rheumatoid arthritis (RA).

Methods: We used data from patients with GCA (1950–2004) and RA (1955–2007) obtained from population-based cohorts. Yearly trends in age-adjusted and sex-adjusted incidence were correlated with the F10.7 index (solar radiation at 10.7 cm wavelength, a proxy for the solar extreme ultraviolet radiation) and AL index (a proxy for the westward auroral electrojet and a measure of geomagnetic activity). Fourier analysis was performed on AL, F10.7, and GCA and RA incidence rates.

Results: The correlation of GCA incidence with AL is highly significant: GCA incidence peaks 0–1 year after the AL reaches its minimum (ie, auroral electrojet reaches a maximum). The correlation of RA incidence with AL is also highly significant. RA incidence rates are lowest 5–7 years after AL reaches maximum. AL, GCA and RA incidence power spectra are similar: they have a main peak (periodicity) at about 10 years and a secondary peak at 4–5 years. However, the RA incidence power spectrum main peak is broader (8–7 years). The short time span of the data, covering 4–11 years, which partly explains the lower correlation between RA onset and AL. The auroral electrojets may be linked to the decline of RA incidence more strongly than the onset of RA. The incidences of RA and GCA are aligned in geomagnetic latitude.

Conclusions: AL and the incidences of GCA and RA all have a major periodicity of about 10 years and a secondary periodicity at 4–5 years. Geomagnetic activity may explain the temporal and spatial variations, including east-west skewness in geographic coordinates, in GCA and RA incidence, although the mechanism is unknown. The link with solar, geospace and atmospheric parameters need to be investigated. These novel findings warrant examination in other populations and with other autoimmune diseases.

INTRODUCTION

Giant cell arteritis (GCA) is a vasculitis primarily of large-sized and medium-sized vessels that occurs in older individuals. GCA incidence rates (1950–1999) show a perplexing temporal cyclical pattern, with regular or semiregular peaks and valleys. Several studies suggested that the environment, including light sensitivity, altitude and latitude, might play a role in the onset of GCA, although the exact environmental causal agent(s) that could account for this cyclical variation in incidence has not been determined. Infectious causes have been inconclusively implicated.

Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting approximately 0.5–1% of the adult population in North


Strengths and limitations of this study

- Our present analysis and previous studies suggest: (1) giant cell arteritis (GCA) and rheumatoid arthritis (RA) incidence rates exhibit solar cycle variations with specific characteristics, that is, the incidences peak 3 years after solar maximum; (2) GCA and RA incidence power spectra have a major peak (periodicity) at 10 years and 8–11 years, respectively, and a secondary peak at 4–5 years; (3) the incidences of GCA and RA increase with increasing latitude; (4) there is an east-west skewness—in the USA, a given RA incidence rate corresponds to a higher geographic latitude on the west coast than in the eastern part of the Midwest and the east coast; and (5) there is weak seasonal variation in the incidence of GCA and juvenile RA.

- None of the leading hypotheses for GCA and RA can account for all five factors listed in (1).

- Geomagnetic activity (AL index) dynamics is consistent with all five factors in (1), although the mechanism has not been fully established.

- The short time span of the data, covering 4–5 solar cycles, may have contributed to the weak statistics. Further studies covering longer time span and geographically diverse locations are needed.

- The present study only examined linear correlations. With larger data sets, future studies can use information theory to investigate non-linear causal–effect relationships.
America and Europe. There is similar evidence of puzzling geographic and temporal variations in the incidence and prevalence of RA. For example, the incidence of RA (1955–2007) exhibits peaks and valleys that appear with some regularity or semiregularity. The incidence of RA appears to be higher with increasing geographic latitude, but the relationship is not straightforward. In the USA, for example, a given OR for the risk of RA in women from the Nurses’ Health Study corresponds to higher geographic latitudes on the west coast than on the east coast or the eastern part of the Midwest. Many studies conclude that these and other geographic and temporal variations in RA incidence and prevalence cannot be explained by genetic factors alone, and suggest that induction of RA is likely influenced by environmental factors or combinations of genetic and environmental factors. However, the exact environmental causal agents responsible for these temporal and spatial variations are unknown.

The periodicities in GCA and RA incidence rates are about 10 and 8–11 years, respectively (shown in Results section). In nature, there is a well-known cycle with an 11-year periodicity: the solar cycle, which refers to the cycle of the number of dark spots on the sun (sunspot number). Many components of solar radiation and solar wind exhibit a solar cycle. For example, the solar extreme ultraviolet (EUV) radiation (wavelength approximately 10–120 nm) varies in phase with the solar cycle, reaching maxima and minima roughly at the same time as sunspot number. The F10.7 index is empirically highly correlated with solar EUV and is often used as a proxy for solar EUV fluxes, although the index does not always track solar EUV perfectly.

Many geospace and upper atmospheric responses also exhibit solar cycle variations, although they may not track sunspot numbers as closely as F10.7 and may vary out of phase with the sunspot number. During magnetically active times, the magnetic and electric fields and electric currents in near-Earth space can undergo rapid fluctuations, which can adversely affect navigation, satellite and wireless communications, power grids, and oil pipelines. One of the processes that can increase the magnetic activity and disturb the Earth’s magnetic and electric fields is the substorm, in which magnetic energy stored in the magnetosphere is released and energises electrons and ions. Substorms occur most frequently in the declining phase of the solar cycle, when the occurrence of the solar wind high-speed stream interfaces is also maximal. Substorm activities can increase the auroral electrojets, particularly the westward electrojet. Auroral electrojets are currents that flow in the ionosphere within the auroral oval, a ring-like structure that hovers a few hundred kilometres above the northern and southern polar regions. The AL index, which is derived from magnetic field perturbations at high latitudes, provides a measure of the strength of the westward auroral electrojet. Lower AL value indicates higher geomagnetic activity and stronger auroral electrojet current.

There have been suggestions that geomagnetic activities have effects on human health, including cardiovascular events such as myocardial infarctions, as well as the modulation of melatonin. In the present study, we investigated whether solar cycle and geomagnetic effects were associated with the incidence of GCA and RA over five decades in a single county in the Midwestern USA.

METHODS

Data on the incidence of GCA and RA for Olmsted County, Minnesota, in (1950–2004) and (1955–2007), respectively, were obtained from prior studies. The yearly average and the yearly 3-year centred moving average of the incidence rates were computed. Incidence rates were age and sex adjusted to US Caucasians in the year 2000.

For our investigation, we chose F10.7 and AL as two representative geospace parameters because they both exhibit a solar cycle, but with differing properties (Introduction section). F10.7 and AL indices for (1950–2007) and (1966–2007), respectively, were obtained from the National Oceanic and Atmospheric Administration (NOAA) Space Weather Prediction Center. Yearly averages of these two geospace indices were computed. Then, lagged correlational analyses of the GCA and RA incidence rates with F10.7 and AL indices were computed. We performed correlational analysis of [X(t), Y(t–τ)], where X=the yearly or the yearly 3-year moving average GCA or RA incidence rate, Y=the yearly average of F10.7 or AL, t=time (year) and τ=lag=0–14 years. We adopt the convention that the correlation is highly significant when p<0.01 (the probability of two random variables giving a correlation coefficient as large as r is <0.01) and the correlation is significant when p<0.05.

AL, F10.7, GCA and RA incidence rates can have multiple frequencies or periodicities. Hence, Fourier analysis was performed to extract this information from these parameters and to determine how similar their power spectra are. In order to better compare the power spectra, the Fourier analysis was performed on the same time interval when all the data overlap, that is, 1966–2004.

RESULTS

Giant cell arteritis

Figure 1A plots GCA incidence rates and the F10.7 record (1950–2004), and figure 1B plots their correlation coefficients (r). The peak correlation of GCA incidence rate (the yearly 3-year moving average) with F10.7 is significant at a lag of 3 years (r=0.28, p<0.05; figure 1B).

Figure 1C plots the two GCA parameters (yearly average and 3-year moving average) and the yearly average AL for the intervals (1950–2004) and (1966–2004), respectively. The correlation of GCA incidence with AL is highly significant at a lag of 0–1 year, for example, GCA incidence peaks 0–1 year after AL reaches a minimum (r=−0.53, p<0.01; figure 1D). The negative correlation indicates that lower AL (ie, higher

Figure 1  Giant cell arteritis (GCA) incidence (1950–2004) and lagged correlations with F10.7 and AL. Yearly average and yearly 3-year moving average of GCA incidence rates are plotted as dotted and solid lines, respectively, in panels (A and C). Their scales are given on the left y-axis label. F10.7 and AL are plotted as dashed lines, and their scales are indicated on the right y-axis in panels (A and C), respectively. The lagged correlations between (yearly average and yearly 3-year moving average GCA incidence rates) and (F10.7 and AL) are plotted as dotted and solid lines in panels (B and D), respectively. The grey lines in panels (B and D) indicate \( r_0 \) such that \(|r|>|r_0|\) (the threshold for significant correlation). The dashed horizontal grey line in panels B and D indicate \( r=0 \).

Figure 2  Rheumatoid arthritis (RA) incidence (1955–2007) and lagged correlation with F10.7 and AL plotted in the same format as in figure 1. Yearly average and yearly 3-year moving average of RA incidence rates are plotted as dotted and solid lines, respectively, in panels (A and C). Their scales are given on the left y-axis. F10.7 and AL are plotted as dashed lines, and their scales are indicated on the right y-axis in panels (A and C), respectively. The lagged correlations between (yearly average and yearly 3-year moving average RA incidence rates) and (F10.7 and AL) are plotted as dotted and solid lines in panels B and D, respectively. The grey lines in panels (B and D) indicate \( r_0 \) such that \(|r|>|r_0|\) (the threshold for significant correlation). The dashed horizontal grey line in panels (B and D) indicate \( r=0 \).
magnetic activity) is associated with higher GCA incidence and vice versa.

**Rheumatoid arthritis**

Figure 2A plots the two RA incidence parameters (the yearly average and yearly 3-year moving average) and the yearly average F10.7. For the yearly 3-year moving average, the correlation of the RA incidence rate with F10.7 peaks at a lag of 3 years, which is significant (r=0.33, p<0.05; figure 2B).

Figure 2C plots the two RA parameters and the yearly average AL, and figure 2D plots their lagged correlations. The correlation of the RA incidence rate with AL is highly significant at a lag of 5–7 years (r=0.49, p<0.01), but note that the correlation is positive (figure 2D).

Instead of using a 3-year moving average, we have also tried to smooth the GCA and RA data using a 3-year moving Hanning algorithm, but the results are not significantly different from those presented in figures 1 and 2.

**Power spectra**

Figure 3A–D plot the power spectra of F10.7, AL, GCA incidence rate and RA incidence rate, respectively. Figure 3A shows that the F10.7 power spectrum peaks at about 10 years, suggesting that F10.7 has a period of about 10 years. The nominal solar cycle period is about 11 years, but there is variability from one cycle to another. Apparently, in the interval (1966–2004), the period is about 10 years, but the power is skewed towards a longer period. In figure 3B–D, the power spectra have significant multiple components, suggesting multiple frequencies or periodicities. The power spectra of AL, GCA incidence rate and RA incidence rate have a secondary peak (periodicities) at 4–5 years, but the F10.7 power spectrum is dominated by a single frequency or periodicity. AL and the GCA incidence rate have a period of about 10 years (figure 3B, C), but the RA incidence rate power spectrum has a broad peak (periodicities) at 8–11 years (figure 3D).

In figure 3B–D, periods greater than 20 years are not shown because they reflect trends rather than periodicities given the limited nature of the data set, which spans about 40 years.

**DISCUSSION**

**Long-term temporal variations**

**Giant cell arteritis**

The lagged correlation between GCA incidence rate and AL reaches a minimum at a lag of 0–1 year, and the correlation is highly significant. This suggests that the incidence of GCA peaks 0–1 year after AL reaches a minimum (the westward auroral electrojet reaches a maximum).

The correlation with solar EUV (F10.7) is not as strong, but it is statistically significant. The two space indices exhibit solar cycle variations and hence are correlated with each other. Thus, the significant correlation between GCA incidence and F10.7 may not necessarily indicate that the solar EUV affects GCA; rather, it may simply indicate that solar EUV correlates with AL. Conversely, the highly significant correlation between the GCA incidence and AL may be at least partly attributed to the F10.7 or some other solar/geo-space parameters that exhibit solar cycle variations. However, as shown in figure 3, the power spectrum for the GCA incidence rate resembles the spectrum of AL more closely than that of F10.7. For example, power spectra for both AL and GCA incidence rate have a main peak at about 10 years and a minor peak at 4–5 years. This minor peak at 4–5 years in AL power spectrum may be attributed to the solar wind high-speed stream interface occurrence rate, which has a small peak near the solar minimum or coronal mass ejection occurrence rate that peaks in the rising phase of solar cycle or near the solar maximum. In contrast, F10.7 consists mainly of a single periodicity.

Another key discriminating factor is the lag time in the correlational analysis. The F10.7 peaks around solar maximum, whereas AL reaches a minimum (strongest auroral electrojet) in the declining phase of the solar cycle, a few years after F10.7 reaches a maximum. Consequently, the F10.7 correlation reaches a maximum with a lag of 3 years, while the AL correlation reaches a minimum with a lag of 0–1 year. The non-zero lag may suggest that the effect is cumulative or that there may be a latency between environmental exposure and disease manifestation, related to delay in diagnosis or to the lag time for a complex autoimmune process to result in symptomatic illness onset.

Epidemiological studies of GCA incidence suggest that there is a latitudinal dependence: the incidence increases with increasing geographic latitude. Lack of sunlight or solar UV radiation may explain this latitudinal variation, but solar UVA (wavelength 315–400 nm) and UVB (wavelength 280–315 nm) do not exhibit much solar cycle variation (<2% variation) and hence may not explain the temporal variation of the incidence rate exhibited in figure 1A and 1C. Moreover, solar UV cannot explain the east-west skewness in spatial variation of GCA incidence discussed in Spatial variations (east-west skewness) section. Conversely, if geomagnetic activities, for example, auroral electrojets, play a role in GCA incidence, then it would be expected that the GCA incidence rate would increase with increasing latitude in the manner discussed in Spatial variations (east-west skewness) section and would have a solar cycle variation, which is consistent with the observations.

The Fourier analysis shows that GCA incidence and AL have similar power spectra, for example, they both not only have a major peak at about 10 years but also have a minor peak at 4–5 years. However, their power spectra are not identical, indicating that other factors might influence GCA incidence. For example, the power spectrum for the GCA incidence rate has a small
peak at about 6 years, which is absent in the AL power spectrum.

**Rheumatoid arthritis**
The relationships between RA and the two space parameters are more complex. The correlation between RA incidence rate and F10.7 is similar to that between GCA incidence rate and F10.7 in that both correlations are significant and peak at a lag of 3 years, suggesting that RA and GCA share some of the same dynamics. As mentioned in the Giant cell arteritis section above, the correlation with F10.7 might simply be attributed to the fact that F10.7 and AL have a common driver—the sun. The power spectrum for RA incidence rate resembles the AL spectrum more closely than the F10.7 spectrum, in that the power spectra for both RA incidence rate and AL have a secondary peak at 4–5 years, whereas the F10.7 spectrum does not. This finding suggests closer ties between RA and AL than between RA and F10.7.

The correlation between RA incidence rate and AL is highly significant at a lag of 5–7 years, but the correlation is positive suggesting that the RA incidence rate reaches a minimum 5–7 years (about half a solar cycle period) after the auroral electrojet reaches a maximum. This result is similar to the relationship between GCA incidence and AL. However, the correlation between RA incidence rate and AL at a lag of 0–1 year is not as strong as that between the GCA incidence rate and AL, suggesting that the effects of auroral electrojets might link more strongly to the decline than the rise in the RA incidence rate. The weaker link between AL and RA onset could be attributed to the fact that RA has multi-periodicities of 8–11 years, whereas AL has a distinct periodicity of 10 years (the AL power spectrum has a sharp peak at about 10 years, whereas the RA incidence rate power spectrum has a broad peak at 8–11 years, as shown in figure 3). The broad peak in the power spectrum for RA incidence rate might indicate that the onset of RA may be linked to additional factors. For example, previous studies have shown that a number of genetic factors, additional environmental factors or combinations of genetic and environmental factors can influence the development of RA.4 5 8 9

**Spatial variations (east-west skewness)**

**Rheumatoid arthritis**
If geomagnetic activities, for example, auroral electrojets, play a role in RA incidence, then it would be expected that the spatial distribution of RA incidence would more strongly correlate with geomagnetic rather
than geographic coordinates, because the auroral oval and auroral electrojets tend to align more along geomagnetic latitude than geographic latitude. This dependence implies an east-west skewness in the incidence rate. In the USA, this means that a given RA incidence rate would be expected to correspond to a lower geographic latitude on the east coast and eastern part of the Midwest than on the west coast, which has been reported.

To illustrate, figure 4A shows the Altitude-Adjusted Corrected Geo-Magnetic (AACGM) coordinates, one of the geomagnetic coordinate systems most commonly used in space physics studies. The auroral oval, where auroral electrojets are frequently found, typically resides at a geomagnetic latitude of 60°–70°, but the auroral oval can expand towards the equator down to 50° or lower during magnetically active times. The probability of encountering the auroral oval increases with increasing geomagnetic latitude, up to approximately 60°–70°. There is an east-west skewness. For example, Washington DC and San Francisco are located at geographic latitudes of ~38.9° and ~37.8°, respectively, (near the middle green line in figure 4A) but their corresponding geomagnetic latitudes are ~50.1° and ~43.2°, respectively. Thus, geographically, Washington DC is only ~1° further north than San Francisco, but geomagnetically Washington DC is ~7° further north than San Francisco.

Figure 4B shows the spatial variation of the risk of RA overlaid with contours of AACGM geomagnetic latitude. The regions with OR>2 (red) are found at higher geographic latitude on the west coast than on the east coast and eastern part of the Midwest. However, in AACGM coordinates, these regions are neatly confined to geomagnetic latitudes poleward of 52.5°, except for the red region in West Virginia, Kentucky and Ohio. The RA cases in these three states may exhibit different properties than the ones at higher latitudes.

One of the leading hypotheses for the cause of RA is lack of sunlight (UVA and/or UVB) resulting in vitamin D deficiency. This may explain the higher RA incidence rate with higher geographic latitude. However, this hypothesis cannot explain the reported east-west skewness (figure 4B) nor can it explain the temporal variation (figures 2 and 3D) because the solar cycle variations in UVA and UVB are less than 2%. If sunlight was the only factor, then we would expect the OR in southern Wisconsin and Michigan to be the same as that in northern California and southern Oregon, but this is not the case (figure 4B). Moreover, if sunlight was the only factor, then RA incidences and prevalences in the USA should be similar to those in southern Europe.

Figure 4 (A) Altitude Adjusted Corrected Geo-Magnetic (AACGM) coordinates in grey lines overlaying Earth’s continents with country boundaries drawn. The numbers in red indicate the latitude and longitude of AACGM. The geographic latitudes (eg, green lines) and longitudes are parallel to the x and y-axes, respectively. USA shares the same geographic latitudes as southern Europe and north Africa, but northern USA shares the same geomagnetic latitudes as northern Europe. (B) Inset showing AACGM latitudes (solid black lines) overlaying spatial variation in RA risk in the USA (adapted from Vieira et al); reproduced with permission from Environmental Health Perspectives. The geographic latitudes are parallel to the x-axis, for example, the dashed green horizontal lines. The OR increases with increasing geographic latitude, but there is an east-west skewness. OR>2 (red) is found at higher geographic latitude on the west coast than in the eastern part of the Midwest and the east coast. However, in geomagnetic coordinates, these regions are generally within the same latitudes (poleward of 52.5°), except for the region in West Virginia, Kentucky and Ohio.
because these regions share similar geographic latitudes (figure 4A). However, they are similar to those in northern Europe, which shares similar geomagnetic latitudes as northern USA (figure 4A). Other leading identified risk factors for RA, including smoking, air pollution, periodontal disease, occupational exposures to silica and low oestrogens, cannot easily explain the spatial or the temporal variations. One caveat is that latitude is somewhat confounded with locations where people of Scandinavian or northern European descent live (the data for the present study were obtained from Olmsted County, Minnesota, where the population is mostly Caucasian). Thus, we cannot rule out the influence of genetics. However, neither race nor latitude alone can explain the temporal variations in RA and GCA incidence rates shown in figures 1A, 2A, 3C, D.

Giant cell arteritis
Similarly, GCA incidence rates in Minnesota (USA) and northern Europe are higher than those in southern Europe and Israel. If sunlight was the causal mechanism, then the GCA incidence rates in Minnesota and southern Europe should be similar because they share similar geographic latitudes, but this is not the case. If geomagnetic activity plays a role in the onset of GCA, then the incidence in Minnesota should be similar to that in northern Europe, consistent with observations, because these regions share similar geomagnetic latitudes (figure 4A). Moreover, Baldursson et al reported that Iceland has the highest GCA incidence rate among those regions sharing similar geographic latitudes (figure 4A). Therefore, Baldursson et al reported that Iceland has the highest GCA incidence rate among Minnesota, Europe, and Israel, which may be expected based on Iceland’s geomagnetic latitude. Iceland is located at geomagnetic latitude of 60°–70° (figure 4A) where auroral oval and electrojets are nominally located.

Seasonal variations (short-term temporal variations)
The geomagnetic activity peaks at the spring and fall equinoxes, a phenomenon known as the Russell-McPherron effect. If geomagnetic activity plays a role in the onset of GCA and RA, then it would be expected that their incidence rates would have a seasonal variation. However, the Russell-McPherron effect on RA and GCA would be weak if the geomagnetic effect was cumulative or if there were delays in reporting the diagnoses. Petursdottir et al reported that the monthly biosympo- positive GCA incidence peaks in March and September–October in a study involving 665 patients over a period of 20 years in Sweden (see their figure 2). Feldman et al reported that in the Prairie region in Canada, the juvenile RA incidence rate has small peaks in the fall and spring. The seasonal variations in the incidence of GCA and RA need further investigation.

FUTURE RESEARCH DIRECTIONS
Taken together, our present analysis and the previous studies suggest that the causal mechanism(s) of RA and GCA should account for the following observations:

(1) GCA and RA incidence rates exhibit solar cycle variations with specific characteristics, that is, the incidences peak 3 years after solar maximum; (2) GCA and RA incidence power spectra have a major peak (periodicity) at 10 and 8–11 years, respectively, and a secondary peak at 4–5 years; (3) the incidences of GCA and RA increase with increasing latitude; (4) there is an east-west skewness—in the USA, a given RA incidence rate corresponds to a higher geographic latitude on the west coast than in the eastern part of the Midwest and the east coast; and (5) there is weak seasonal variation in the incidence of GCA and juvenile RA.

None of the leading hypotheses for GCA and RA, namely, lack of sunlight (including solar UV), vitamin D deficiency, smoking, air pollution, periodontal disease, occupational exposures to silica and low oestrogens, can account for all five factors listed above. Our analysis shows that these five factors are consistent with the effects of geomagnetic activity (AL index).

Although the mechanism for this geomagnetic effect has not been established, one possibility is that geomagnetic disturbances result in reduced melatonin excretion. Burch et al found that on days when geomagnetic activity was high, the mean excretion of the overnight melatonin metabolite (6-OHMS) was approximately 21% lower than on days when geomagnetic activity was low, in a study of 142 male electric power workers who were exposed to ambient light and a magnetic field generated from 60 Hz electric power. Melatonin has been shown to act as an anti-inflammatory agent and generally has an immune-enhancing effect in many species, including humans, by providing a circadian immunoregulatory signal to the immune system. Melatonin scavenges and inactivates oxygen-derived free radicals (reactive chemical species with unpaired electrons in their outer orbitals), such as, ONOO⁻, and OH, all of which have been found at the site of inflammation. Remans et al also reported the association of free radicals and RA. Esquifino et al found that daily injections of melatonin restored the inflammatory response in old rats to the level found in young rats. Further mechanistic studies of the effects of geomagnetic activity are needed.

A geomagnetic disturbance, such as the substorm, introduces temporal variations in the magnetic and electric fields in the ionosphere in the vicinity of the auroral oval, which can drive transient currents in the ionosphere, for example, auroral electrojets, which in turn can drive currents within the Earth due to its high conductivity. The observed fluctuating electric and magnetic fields on the ground is a combined effect of the fluctuating electric currents in the ionosphere and the induced currents flowing within the Earth. On the ground, the Earth’s main magnetic field is much stronger than the magnetic field induced by geomagnetic activities. However, Palmer et al reported studies that hypothesised that a weak, rapidly fluctuating magnetic field and electric current may increase free radical formation, which impacts negatively on inflammation. Further investigation is needed to...
determine whether the magnitude and frequency of the geomagnetically induced magnetic field fluctuations would produce an effect similar to that discussed by Palmer et al\textsuperscript{8} with consideration of the precise molecular effects at a biological level in vivo or in vitro.

If the auroral electrojets play a role in the development of RA and GCA, then statistically their incidence rates would increase with increasing geomagnetic latitude; however, the rates would reach a maximum at a ‘maximum latitude’, poleward of which the rates would decrease. For example, poleward of the auroral oval, nominally at geomagnetic latitude $\sim70^\circ$, the incidence rates should decrease with increasing latitude. However, the maximum latitude could be $<70^\circ$, depending on a few parameters, such as how often the auroral oval expands towards the equator and the strength of the electrojets.

The present study does not rule out the possibility that there could be other parameters that exhibit solar cycle variations that can be linked with RA and GCA. The highly significant correlation between RA and GCA incidence rates with AL might be the manifestation of a causal agent that also exhibits solar cycle variation. Two examples are given next.

The cloud cover modulates the solar UV radiation that reaches the ground at sea level. If the cloud cover has a solar cycle variation, then it may lead to a solar cycle variation in melatonin production in human body. Some studies suggested that 3–4% variation in global cloud cover can be linked with cosmic rays with both parameters vary out of phase with the sunspot number (cloud cover reaches a minimum during solar maximum).\textsuperscript{40} However, other studies found that there is no clear cosmic rays-cloud link globally, although there may be a weak link regionally.\textsuperscript{41, 42} In any case, the dominant variation of the solar UV irradiance at sea level is the seasonal variation with a maximum in the summer and a minimum in the winter. So, if solar UV (through the cloud) is the primary causal agent in RA and GCA incidence, then incidence rates would have one peak per year, but Petursdottir et al.\textsuperscript{26} and Feldman et al.\textsuperscript{20} reported two peaks per year (Seasonal variations (short-term temporal variations) section).

Solar UV and cloud may have some role in the GCA and RA incidence, but their exact roles need further investigation.

Variation of the cloud cover may be associated with the Earth surface temperature variation. Indeed, the surface temperature exhibits solar cycle variations, but the difference in temperatures between solar maximum and solar minimum is about $0.2^\circ K$\textsuperscript{43} Further, the surface temperature peaks around the solar maximum, which suggests that there would be a 3-year lag between RA and GCA incidence and surface temperature. Like cloud cover, the dominant variation in temperature is the seasonal variation: the temperature peaks once a year in the summer. Other solar, geospace and atmospheric parameters need to be considered and investigated in future studies.

The present study analysed data from only one location, namely, one county in southern Minnesota. The short time span of the data, covering only 4–5 solar cycles, may have contributed to the weak statistics. Future studies should analyse RA and GCA data covering a longer interval from many locations and organise them in geomagnetic coordinates such as AACGM.\textsuperscript{23} With a larger data set, one can use information theory to investigate non-linear causal–effect relationships.\textsuperscript{11, 12, 41}

Our findings suggesting solar cycle and geomagnetic effects on the incidences of RA and GCA warrant further study to confirm these associations and to explore their biological and clinical implications in other populations and other autoimmune diseases.

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Contributors SW and JRJ performed the data analysis and interpretation of temporal and spatial variations in RA and GCA, and a possible link to solar cycle. SEG, LGR, FWM, CSC and ELM provided the RA and GCA background. SEG, JMC and ELM contributed to the RA and GCA data. All authors were involved in the writing and revisions of the manuscript and approval of its submission.

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Data sharing statement All data used in the study are publicly available. All the derived data used in the study will be made available on request.

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