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Seasonality of meningitis in Africa and climate forcing: aerosols stand out

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Bacterial meningitis is an ongoing threat for the population of the African Meningitis Belt, a region characterized by the highest incidence rates worldwide. The determinants of the disease dynamics are still poorly understood; nevertheless, it is often advocated that climate and mineral dust have a large impact. Over the last decade, several studies have investigated this relationship at a large scale. In this analysis, we scaled down to the district-level weekly scale (which is used for in-year response to emerging epidemics), and used wavelet and phase analysis methods to define and compare the time-varying periodicities of meningitis, climate and dust in Niger. We mostly focused on detecting time-lags between the signals that were consistent across districts. Results highlighted the special case of dust in comparison to wind, humidity or temperature: a strong similarity between districts is noticed in the evolution of the time-lags between the seasonal component of dust and meningitis. This result, together with the assumption of dust damaging the pharyngeal mucosa and easing bacterial invasion, reinforces our confidence in dust forcing on meningitis seasonality. Dust data should now be integrated in epidemiological and forecasting models to make them more realistic and usable in a public health perspective.

1. Introduction

Bacterial meningitis (which we will refer to as meningitis) is a contagious disease transmitted from individual to individual by airborne droplets of respiratory or throat secretions. The highest burden of the disease occurs in the 'African Meningitis Belt', a region stretching from Senegal to Ethiopia with an estimated population of 300 000 million people [1,2]. While *Neisseria meningitidis* A is the main cause for large epidemics, serogroups W135, C and X are also responsible for localized outbreaks [3,4] as well as *Streptococcus pneumoniae* or *Haemophilus influenzae* type B. Increase in incidence is typically observed every dry season, with weekly incidence rates reaching up to 100 per 100 000 population in individual communities [5,6]. Even with appropriate treatment, the mortality rate fluctuates around 10 per cent, and 10–15% of survivors suffer long-term neurological sequelae [7]. Asymptomatic carriage is common, which most often does not lead to the consecutive development of the illness [8,9]. Despite a strong seasonality, the determinants of meningitis dynamics are still poorly understood. Various factors are likely involved in the underlying mechanism of the disease dynamic, including (re)introduction of consecutive strains [6,10], vaccination impact, population dynamics and immunity [11–13]; climate and dust are often advocated as having a large impact. The epidemic season for meningitis coincides with the dry season and ends with the arrival of the African monsoon [1,2,14]; early epidemic onset often correlates with high annual incidence [15].

A bimodal tropical climate is predominant in Western Africa, with a dry season running from mid-October to mid-April followed by a wet season over the remaining six months of the year [16,17]. In the core of the dry season, from January to March, the dry and hot winds called Harmattan blow from the northeast and carry high dust loads [18]. These dusts mostly originate from Bodélé (Chad) [19] and are carried by wind over continental distances. Their specificity is to be mainly localized in the low layers of the atmosphere [20]. During the wet season, the southern monsoon winds blow from the Gulf of Guinea, and bring precipitations (mostly July–September) and high levels of humidity. Temperature, humidity levels, pressure, wind and dust thus display seasonal variations. This seasonality is less obvious in the arid Sahara region where it is mostly dry the whole year, as the monsoon winds do not go beyond 13.5° of latitude at their maximal northward expansion. In the meantime, rainfalls occur in areas up to 16° of latitude, with a gradient in their frequency and intensity.

The influence of climate on meningitis dynamics was first suspected in 1940 by Sicé *et al.* [21]. Since then, several studies have investigated the relationship between climate and meningitis using different approaches: qualitative [1,2,5, 6,22,23] and recently quantitative [24–28]. The main conclusions of these studies were that (i) the intensity of the epidemics is related to the Harmattan wind [23,24,27,28] and its strength [29]; (ii) the onset of the epidemics is in phase with the winter maximum as defined by Sultan *et al.* [24] and with the arrival of the dust in the low layers of the atmosphere [25,26]; and (iii) the end of the epidemic season coincides with the arrival of the African monsoon [25,26]. The main hypothesis to explain climate impact on meningitis epidemics is an increase in the invasion rate (i.e. shift from carrier to infected status) [10]: persistent low air humidity and high dust loads are believed to damage the pharyngeal mucosa and ease the colonization of the epithelium by the meningococci [5,6,8,14]. Additionally, increased incidence could be attributed to higher transmission levels, due for instance to changes in living habits, such as proximity of individuals as they take refuge from the dusty winds [6,29]. Finally, co-occurrence of viral respiratory infections is expected to weaken the immune system and further ease the transmission and invasion by the bacteria [22].

To our knowledge, all studies of climate impact on meningitis were conducted at the national level and the annual or monthly time scale. Here, we focused on a finer level: the weekly temporal scale and district spatial scale, which are currently used for operational decisions and in-year response to emerging epidemics in most countries of the Belt, following WHO recommendations [30]. Two factors characterize an epidemic: its timing and its amplitude. In this study, we focused on the timing aspect and explored the relationship between the seasonality of meningitis, dust and climate. Based on wavelet and phase analysis [31], we investigated and compared time-varying periodic components, and mostly searched for temporal and spatial consistency in the time-lags between the signals, in order to detect persistent links. On top of dust, the climatic variables we have considered are: temperature (TEMP), wind force (Wf), wind direction (Wd) and relative humidity (RH). Niger was selected to conduct this analysis as it is one of the most affected countries of the Belt and has the longest history of meningitis cases reporting. As the district-level weekly scale is currently used for operational decisions, detailed understanding of the relationship between meningitis and climate as well as dust could help in improving the public health response strategy.

2. Data and methods

2.1. Data

The epidemiological data consist of reported number of suspected meningitis cases per week from 1986 to 2007, for Niger's 38 health districts (figure 1). Data were collected through the national enhanced surveillance system, which is supported by WHO. Suspected cases were identified by use of a standard case definition based on clinical criteria [32].

The aerosol index (AI) is a semi-quantitative index of the aerosol loads integrated over the whole atmospheric column. It is based on ultraviolet radiance measures captured by satellite probes [33,34]. Specificities of the AI product are to be (i) particularly efficient over bright surfaces such as desert [35,36], being thus adapted to our semi-arid area of interest that is Niger and (ii) sensitive to dust altitude, with higher AI values obtained for the same amount of dust at high altitude compared with low altitude [37,38]. The AI product is available from the Total Ozone Mapping Spectrometer (TOMS) at a $1^\circ \times 1.25^\circ$ spatial resolution (1° corresponds to approx. 100 km) from mid-1996 to 2005 [33], and from the Ozone Monitoring Instrument (OMI) at a $0.25^\circ \times 0.25^\circ$ spatial resolution from 2005 to 2009 [34]. An instrumental drift was detected for TOMS over the years 2002–2004 (R McPeters, S Taylor, G Jaross, D Haffner, G Labow, M Kowalewski 2007, personal communication; electronic supplementary material, figure S1). Three periods were accordingly defined, 1996–2001 (TOMS), 2002–2004 (TOMS) and 2005–2009 (OMI), over which data were corrected through standardization of the values, using as a reference the annual mean and standard deviation values averaged over the third period. The continuous time series that were obtained are further referred to as DUST.

Only dust at ground level has the potential to be inhaled by humans and to impact their health. We aimed at correcting the AI measurements from an altitude effect in order to better approach levels of dust concentrations at the surface. This is made possible by assuming that the altitude of dust in the Meningitis Belt results from cyclic climate conditions: in the dry season, the dusty Harmattan winds blow at low altitude [20]. It is followed by a transition period between the Harmattan and the monsoon regimes, during which vertical mixing is important, with dusts located both at low and high altitudes. At the beginning of the wet season, the monsoon wind replaces the air at the surface and pushes the dusty air higher up in the atmosphere. Finally, the concentration of dust in the higher layers of the atmosphere further decreases until the arrival of the next dry season. We used measurements of the surface aerosol concentrations extracted from two of the three ground-based stations of the Sahelian Dust Transect. These were set in the frame of the African monsoon multidisciplinary analyses (AMMA) programme, and rely on the tapered element oscillating microbalance technology [18]. The two stations we considered are located in the semi-arid part of Niger and Mali; whereas the third is located in Senegal on the coast, where climate is different. For the two given stations, we compared the related *in situ* measurements (named particulate matters, PM) to DUST values. We showed that, despite a large intra-seasonal variability, the PM/DUST rates could be considered seasonal and were overall

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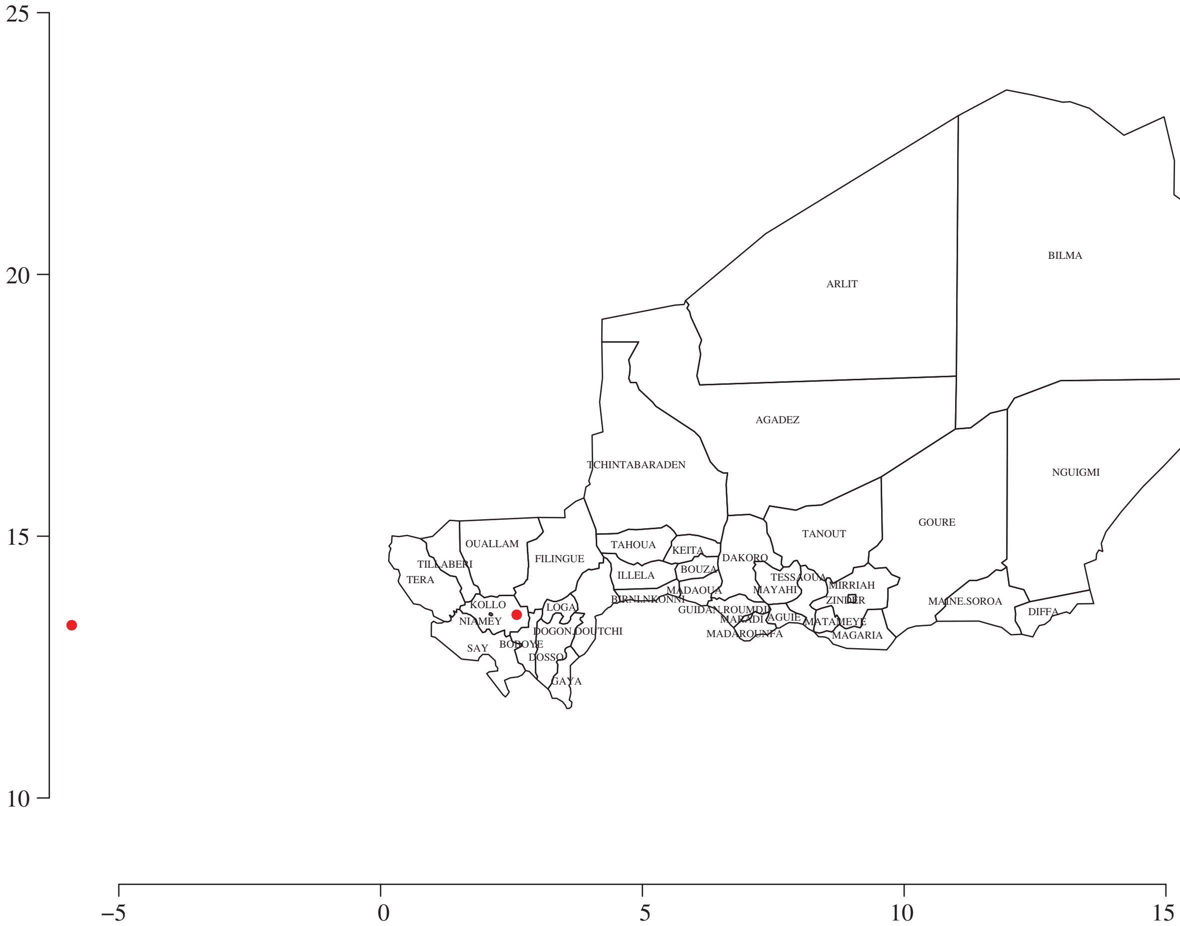

Figure 1. Map of districts in Niger. The country was partitioned into 38 health districts until 2002. After 2002, three of these districts were subdivided, which we did not consider in order to maintain a consistent geography throughout the study period. The right and left dots give the location of the Banizoumbou (Niger) and Cinzana (Mali) ground-based weather stations, respectively. (Online version in colour.)

consistent across years and across the two stations (see the electronic supplementary material, figure S2). An averaged and smoothed annual curve of the PM/DUST rates was computed: it reflects the week-specific proportion of the aerosols that are located at ground level. DUST data were further multiplied by the value of this annual curve for the corresponding week. The resulting time series (referred to as $DUST_C$) represents the aerosols concentrations at ground level better than DUST (see the electronic supplementary material, figure S2, for details of the method). However, the PM/DUST rates are climate-dependent, and our correction is expected to be valid only over the Sahel part of Niger, where the dust cycle is alike. Note that Niger is divided into a northern semi-desert part (typically, Agadez, Arlit and Bilma districts, figure 1), where precipitations do not exceed 200 mm yr^{-1}, and a southern semi-arid part, where they vary between 200 and 600 mm yr^{-1}.

ERA-Interim is the third-generation reanalysis provided by the European Centre for Medium-Range Weather Forecasts [39], from which we have extracted RH, TEMP, Wf and Wd data for the period 1989–2009 at a 1.5° spatial resolution at a daily time-step.

For each climate and dust variable, we used a spatial mask at the given resolution to extract the values of the pixels overlapping each district, which we averaged. Weekly time series were further obtained by averaging the daily values for each calendar week, in agreement with the epidemiological dataset. Time series of meningitis, climate and dust variables are displayed in figure 2.

2.2. Wavelet analysis

Detecting periodicities in time series is classically achieved by frequency decomposition using Fourier transform. This method requires series to be second-order stationary, which most epidemiological or environmental signals are not. On the other hand, wavelet transforms cope with transient dynamics by allowing extraction of periodic components that are time-dependent [31,40]. Wavelet coefficients are the result of the convolution product between the time series and a windowed mathematical function (called the mother wavelet) that is dilated onto the desired wavelike shape and translated across the time axis [41,42]. The relative importance of these coefficients at each time step and frequency is represented on a time–frequency two-dimensional plot called the wavelet power spectrum. The cone of influence is the region that is not influenced by edge effects; outside this region, wavelet coefficients should be interpreted with caution [43]. When a given periodicity is detected, the related phase can be extracted, and indicates the instantaneous position in the cycle.

Statistical significance tests for the wavelet transforms go from simple bootstrap [44] to more complex resampling that preserves the autocorrelation function of the raw time series [45]. In our study, we used beta-surrogates that mimic the

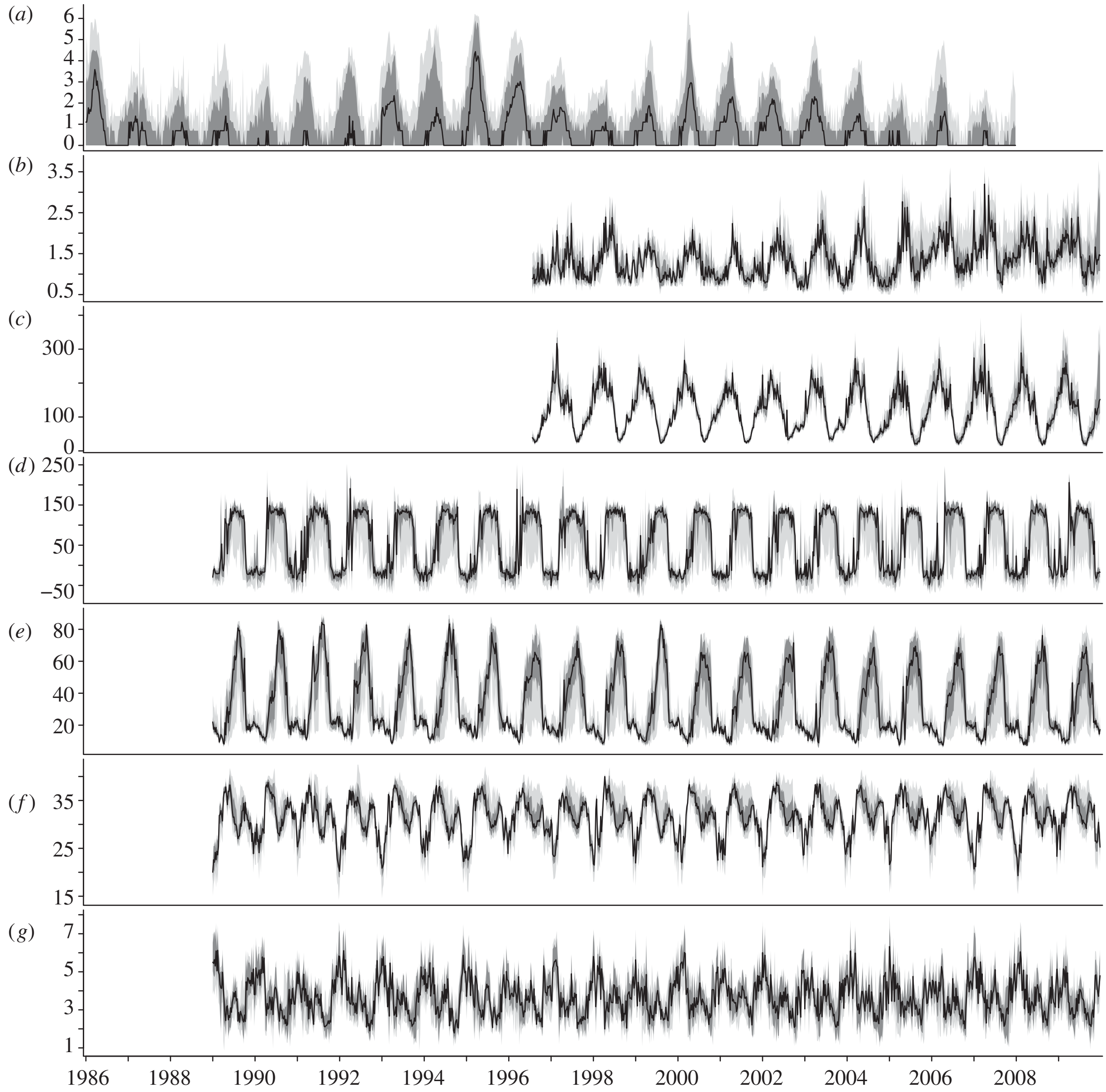

Figure 2. Time series of meningitis (*a*), DUST (*b*), $DUST_C$ (*c*), Wd (*d*), RH (*e*), TEMP (*f*) and Wf (*g*) over the respective study periods. Meningitis time series were log-transformed. The black line depicts the week-specific median value across districts; the dark grey region depicts the area between the week-specific 10% and 90% percentiles; the light grey region depicts the area between the week-specific minimal and maximal values across districts.

slope of the wavelet power spectrum of the original time series, and thus display similar variance and autocorrelation structure [46]. For each test, 1000 surrogates were simulated; significance is given at a 5% confidence level.

2.3. Coherency and phase difference

Wavelet coherency provides information about two non-stationary time series being linearly correlated or not at a particular frequency and temporal location in the time–frequency plane [47]. Coherency coefficients are equal to one when there is perfect linear relationship, i.e. when in a given time period, the two time series oscillate with the same periodicity [31]. Similarly to univariate wavelet spectra, the importance of the coherency coefficients is represented on a time–frequency two-dimensional plot called the coherency graph. Significance is tested by simulating 1000 beta-surrogates for both time series, computing their related coherency graphs and comparing them to the coherency graph of the original data.

When coherency is significant, the phase difference can be interpreted. It represents the instantaneous time lag between the time series' oscillations at a given periodicity. Two time series are phase-locked for a given periodicity when they are coherent and their phase difference is constant throughout the study period. They are synchronous in phase if they are phase-locked with null phase difference, in which case values rise and fall simultaneously [48,49]. For each pair of variables, the phase difference curve was computed for each district and plotted. To estimate the consistency across districts in the evolution of these phase difference time series, we compared the differentiated time series two-by-two (observed within the cone of influence) by defining their correlation coefficients, and retained the mean value. We will refer to this distance as the distance *D*. Similarly to correlation coefficients, the closer to 1 the *D* value, the more consistent the evolution of phase difference across districts.

In our study, we used a Morlet mother wavelet because it is specially suited for sinusoidal signals, which most epidemiological and climate series are [31]. Phase difference values are, however, not expected to differ whichever

Table 1. Characteristics of the phase difference curves between DUST, $DUST_c$ and climate variables. Phase differences for Aguié and Bilma are not accounted for, as they are considered as extreme values (see electronic supplementary material, figures S7 and S8, for details).

	mean	range	s.d.	mean weekly s.d.	distance *D*
DUST versus Wd	−10.01	(−17.60, −2.25)	3.08	2.47	0.85
DUST versus RH	−13.81	(−21.50, −6.43)	2.92	2.21	0.88
DUST versus TEMP	−3.61	(−12.40, 4.79)	3.25	2.47	0.89
DUST versus Wf	12.38	(−1.28, 22.29)	4.22	3.69	0.65
$DUST_C$ versus Wd	−17.14	(−19.65, −11.42)	1.42	0.94	0.92
$DUST_C$ versus RH	−20.95	(−25.23, −15.22)	1.43	0.89	0.97
$DUST_C$ versus TEMP	−10.74	(−17.73, 0.20)	2.93	2.65	0.91
$DUST_C$ versus Wf	5.26	(−3.19, 11.87)	2.76	2.52	0.58
Wd versus RH	−3.93	(−8.25, −2.87)	0.76	0.71	0.72
Wd versus TEMP[a]	5.99	(−0.57, 11.92)	2.45	2.38	0.76
Wd versus Wf	22.25	(14.24, 26.55)	2.40	2.21	0.71
RH versus TEMP[a]	9.93	(5.38, 15.03)	2.07	1.99	0.73
RH versus Wf	26.18	(17.82, 31.98)	2.52	2.34	0.77
TEMP versus Wf[a]	16.34	(4.36, 24.69)	3.93	3.84	0.66

[a]Phase difference for Gaya is not accounted for.

mother wavelet is considered. Wavelet methods were directly applied on climate variables, whereas log-transformation was first performed on the meningitis time series to bring out their periodicity by compressing extreme values.

Wavelet spectra and coherency graphs could not all be presented. Instead, we selected a district that displays average characteristics, for which graphs are given as an example in the electronic supplementary material, figures S3 and S4. Districts' locations are given in figure 1.

3. Results

3.1. Univariate wavelet spectra

Among the 38 districts of Niger, five recorded very low meningitis incidence with numerous zero values: Arlit, Bilma, Diffa, Maine-Soroa and N'Guigmi. This leads to unclear seasonality and makes the time series inappropriate for wavelet analyses. These five districts are located in the arid northwest part of the country. Their low incidence is likely partly due to their small population size (see the electronic supplementary material, figure S5). For all other districts, meningitis time series are dominated by an annual periodic component, which is significant—except when incidence is too low (example of wavelet spectrum given in the electronic supplementary material, figure S3*a*). Transient pluri-annual periodicities were identified, with a dominant 6–8 years cycle displayed in half of the districts' spectra. Broutin *et al.* previously highlighted an 8–12 years transient periodic component for meningitis epidemics at a national level, in nine countries of the Meningitis Belt including Niger [50]. The time series used in our study were of too short a length to test the persistence of these low-frequency components at a district level.

For all the districts, spectra for DUST, $DUST_C$, RH and Wd exhibited a dominant annual periodicity, significant over the whole study period—except for Arlit, Bilma and Aguié for Wd, and to a lower extent for RH (example given in the electronic supplementary material, figure S3*b*–*f*). This annual periodicity is also displayed in Wf and TEMP spectra; it is, however, not significant over the whole study period, and is counterbalanced by a strong six-month periodicity, mostly for TEMP. This periodicity is due to the occurrence of two consecutive climate regimes in the area of study: the Harmattan regime in the dry season, with a maximum in Wf and in TEMP being reached in March; and the monsoon regime, with local maxima in Wf and TEMP reached in July (figure 2*e*,*f*; averaged patterns in electronic supplementary material, figure S6). A six-month periodicity also appears in several districts' RH spectrum, yet in a weak and non-consistent way. No pluri-annual periodicities were observed in any of the dust or climate spectra.

We further observed the temporal evolution of the significance of the annual periodic component. High significance for a given parameter corresponds to large amplitude between values of the dry and the wet season. Interestingly, we noted a decrease in the significance of the RH annual periodicity in northern districts: the rainy season's average RH decreased in these districts after the year 2000. In the following, we focus on the dynamics of the predominant 1-year periodic component as we aim at better understanding the impact of dust and climate factors on the seasonality of the disease.

3.2. Coherency and phase difference

First, we observed the district-level coherency and phase difference for each pair of dust and climate variables (results summarized in table 1). On the annual periodicity, coherency was significant over the whole study period for all districts and all pairs of variables. Results highlighted a synchronicity in phase for Wd versus RH in all districts but Arlit and Bilma (table 1, mean and s.d.). The temporal evolution of the phase difference was similar across the same districts for DUST versus TEMP, RH and Wd (distance *D* values greater than 0.85), and to a greater extent for $DUST_C$ versus TEMP, RH

Table 2. Characteristics of the phase difference curves for meningitis (men) versus dust and climate variables. Phase difference was considered for all districts but the low incidence ones.

	mean	range	s.e.	mean weekly s.e.	distance D
men versus DUST	−5.87	(−11.96, 1.94)	2.22	1.79	0.62
men versus $DUST_C$	1.55	(−4.49, 7.30)	1.95	1.68	0.55
men versus Wd	−15.38	(−33.50, −8.13)	2.21	2.17	0.15
men versus RH	−19.66	(−36.98, −11.40)	2.77	2.76	0.12
men versus TEMP	−9.07	(−31.02, 1.18)	3.05	2.95	0.31
men versus Wf	6.54	(−12.12, 15.88)	3.26	3.11	0.31
men versus Wd[a]	−15.16	(−19.66, −8.13)	2.10	2.11	0.11
men versus RH[a]	−19.33	(−32.50, −11.40)	2.82	2.84	0.11
men versus TEMP[a]	−8.54	(−16.29, 1.18)	2.96	2.91	0.45
men versus Wf[a]	6.98	(−2.44, 15.88)	3.49	3.35	0.45

[a]Computed over the period all data were available (i.e. 1996–2007).

and Wd (D values greater than 0.90); yet it could not be considered phase-locked (too large s.d., table 1).

Second, coherency and phase difference were computed for meningitis compared to dust and climate variables for all but the five low incidence districts previously defined (results summarized in table 2). Coherencies are all dominated by a 1-year periodic component, significant over the whole study period for meningitis versus DUST, $DUST_C$, RH and Wd, and in a more inconsistent way for meningitis versus TEMP and Wf (example of coherency graph given in the electronic supplementary material, figure S4). Over the respective study periods, we observed no district-level phenomenon of phase lock, but a noticeable consistency in the evolution of the phase difference curves across districts for meningitis versus DUST and $DUST_C$: unlike other variables, the phase difference evolves similarly across districts (figure 3). The value for the distance D is 0.62 for meningitis versus DUST and 0.55 for meningitis versus $DUST_C$; it does not exceed 0.31 for meningitis versus other climate variables. We further computed the distance D over a common restricted time period over which DUST and $DUST_C$ are defined. Over this 11 year period, the D value for meningitis versus climate variables does not exceed 0.45, hence remains smaller than the 0.62 and 0.53 values for DUST and $DUST_C$, respectively. On average, the time lag between seasonal components of meningitis and DUST is −5.87 weeks, and 1.55 weeks for $DUST_C$. The averaged phase difference was observed by district and displayed spatial variations (figure 4). We further observed the phase difference between districts for a given variable: the closer to 0, the more similar the timing of the cycles between districts. The global standard deviation of these two-by-two phase difference curves is 2.91 for meningitis (table 3); it is 2.22 and 1.95 for meningitis versus DUST and meningitis versus $DUST_C$, respectively (table 2). This indicates there is a stronger similarity when relating a district's meningitis curve to its DUST or $DUST_C$ curves than when relating it to other districts' meningitis curves. Moreover, the standard deviations of the two-by-two phase difference curves for DUST and $DUST_C$ are 3.74 and 1.28, respectively (table 3). Despite the small variability between districts for $DUST_C$, comparing $DUST_C$ to meningitis curves led to a smaller variability than comparing meningitis curves together.

4. Discussion

Relationship between climate and dust and meningitis has often been advocated in the last decade. First quantitative studies were recently conducted, especially in the frame of the AMMA programme [24–27], leading to new hypotheses on the relationships between climate, dust and epidemic cycles. In this study, we strengthen these first results and go further into details by considering data at the weekly district level. To our knowledge, despite being the base for in-year response to emerging epidemics in most countries of the Belt, this scale has not been used yet for investigating meningitis epidemics' link with climate and dust. Wavelet methods were recently largely used in both epidemiology [50–54] and climate [55,56], and were first applied to meningitis data by Broutin *et al.* [50] at a national scale to compare periodicities and detect synchrony between nine countries of the Meningitis Belt. In our study, we used this method to investigate climate forcing on meningitis seasonality, and mostly focused on detecting spatially consistent time-lags between the seasonal component of the signals. Results highlighted the special case of dust in comparison to Wd, humidity or TEMP: the time-lags between seasonal components of meningitis and DUST and between meningitis and $DUST_C$ evolve similarly for all districts (figure 3). This favours the assumption of a strong link between dust and meningitis annual seasonality and prompts considering dust as a major predictor of the timing of meningitis epidemics.

Despite this consistency across districts, the time lag between the seasonal component of dust and meningitis evolves across the study period: this is likely due to another time-varying factor, which is that interaction with dust would trigger an increase in meningitis cases. Introduction and re-introduction of consecutive meningitis strains [14,57] in the area of study could be this other predictor: with an increased global susceptibility of the population to these new strains, dust could have a more instantaneous effect by helping the invasion of the given bacteria, with it being hardly slowed down by the immune system. Another candidate predictor could be the intensity of dust events; but they do not appear to covary with the average difference of phase (figure 2*b* versus figure 3*a* and figure 2*c* versus figure 3*b*). However, the effect of dust and climate variables on the amplitude of the

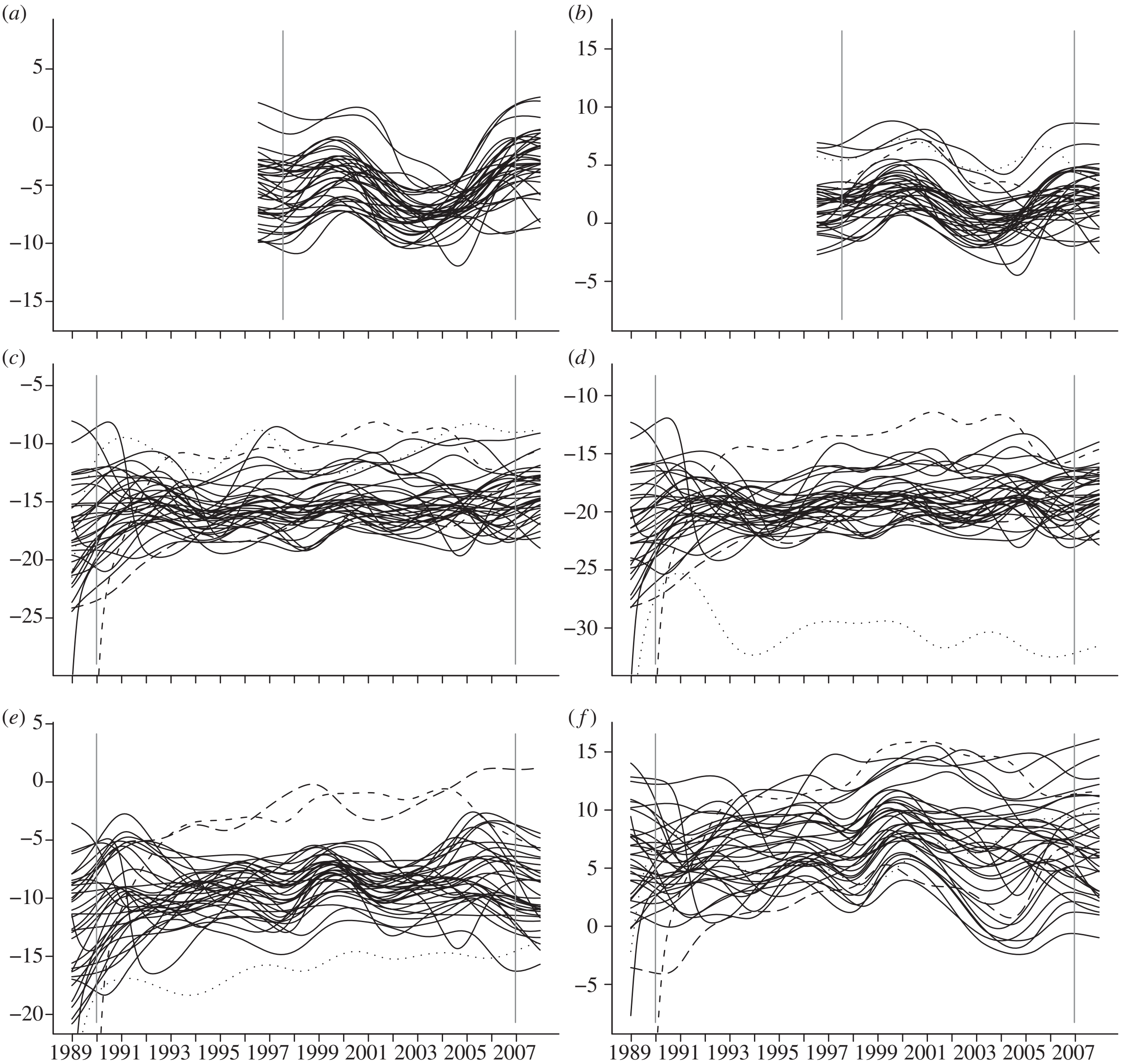

Figure 3. District-level curves of phase difference for the annual periodicity as a function of time (1989–2007) for meningitis log-transformed time series compared with DUST (*a*), DUST$_C$ (*b*), Wd (*c*), RH (*d*), TEMP (*e*) and Wf (*f*). The *y*-axis gives the phase difference in weeks. Same scales are used for all graphs. Grey vertical lines mark the boundaries of the cone of influence. The five low incidence districts (Arlit, Bilma, Diffa, N'Guigmi and Maine-Soroa) are not represented here. In graph (*b*), the dashed line depicts Agadez, the dotted line Gouré. In graphs (*c*), (*d*), (*e*) and (*f*), the dashed line depicts Agadez, the dotted line Aguié and the long-dashed line Gaya.

epidemics was not investigated here (as we focused on the seasonality), and should be studied in more depth.

Only dusts at ground level are of interest for the public health community for being potentially inhaled by local population and impacting human health. However, remote sensed AI corresponds to absorbing aerosols cumulated over the whole atmospheric column: we aimed at correcting the AI estimates (so-called DUST) from an altitude effect in order to be more representative of the dust at the surface (so-called DUST$_C$). Same spatial consistency in the evolution of the phase difference with meningitis was observed for DUST$_C$ and DUST, with a negative average lead time for DUST (−5.81 weeks), while it is positive for DUST$_C$ (1.53 weeks, table 3). This difference reflects the increase of aerosol altitude at the end of the meningitis season [37,38]. These results reinforce our confidence in using our correction of the AI estimates of dust: the pattern of similarity among districts in the evolution of the phase difference observed for DUST versus meningitis is reproduced for DUST$_C$ versus meningitis; the average phase difference becomes positive, but its variability is maintained (table 3). This indicates that the applied correction was not too strong and did not constrain all district-level annual curves to peak simultaneously. The average phase difference between DUST$_C$ and meningitis is 11 days, which is consistent with the time for dust to damage the respiratory tract along with the incubation period of the disease (1–14 days) [58]. This study hence suggests that, when the levels of dust in the low layers of the atmosphere start increasing/decreasing, we can infer that the meningitis incidence will start increasing/decreasing approximately 10 days later. As specified previously, another time-varying factor (possibly (re)introduction of consecutive strains) is believed to interact with dust, and define the exact time lag between dust and meningitis oscillations.

The remaining variability among districts in the average phase difference between dust and meningitis (figure 4) could be due (i) to the local intensity and persistence of dust events; (ii) to reporting delays with longer delays expected in

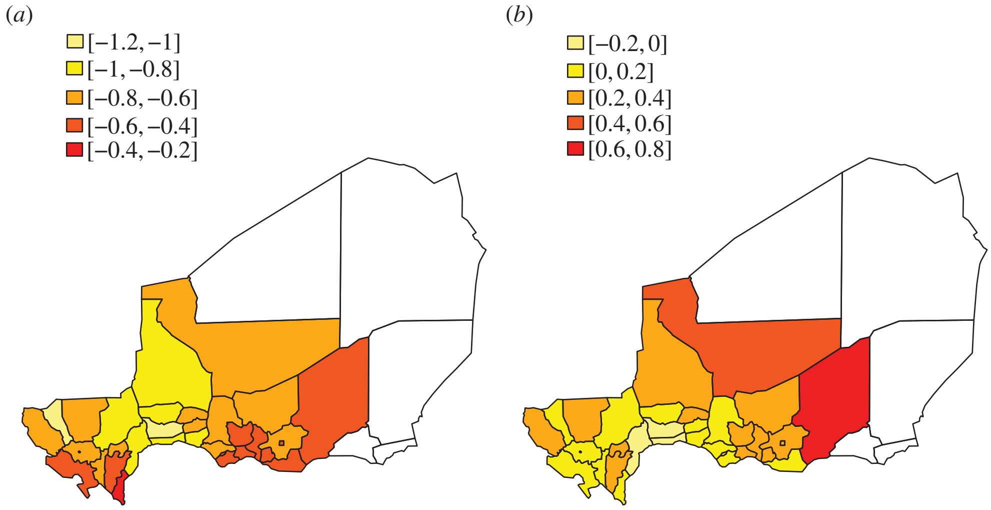

Figure 4. Map of district-level average phase difference for meningitis versus DUST (*a*) and meningitis versus $DUST_C$ (*b*) over the period 1996–2007. All districts are considered except the five low incidence districts. (Online version in colour.)

Table 3. Characteristics of the phase difference curves between districts for a given variable among meningitis (men), dust and climate.

	mean	range	s.e.	mean weekly s.e.
men[a]	−0.26	(−11.78, 11.32)	2.91	2.88
DUST	0.32	(−11.59, 14.43)	3.74	3.70
$DUST_C$	0.18	(−4.16, 5.03)	1.28	1.27
Wd	−0.58	(−8.88, 8.26)	1.85	1.82
RH	1.00	(−15.61, 15.92)	3.51	3.41
TEMP	−0.24	(−15.79, 16.94)	4.38	4.36
Wf	−0.11	(−10.10, 10.10)	3.00	2.89
men[a,b]	−0.28	(−9.93, 10.83)	2.91	2.90
DUST[b]	0.26	(−10.74, 12.84)	3.56	3.53
$DUST_C^b$	0.19	(−4.16, 5.03)	1.31	1.29
Wd[b]	−0.58	(−8.88, 8.26)	1.81	1.77
RH[b]	1.17	(−15.47, 15.92)	3.95	3.93
TEMP[b]	−0.22	(−15.79, 16.75)	4.47	4.46
Wf[b]	−0.13	(−9.96, 9.58)	3.16	3.06

[a]Phase difference for all districts but the low incidence ones (i.e. Arlit Bilma, Diffa, N'Guigmi and Main-Soroa).
[b]Computed over the period all data were available (i.e. 1996–2007).

remote districts; (iii) to spatial variations in the susceptibility, resulting from contrasted socio-cultural and environmental factors; and/or (iv) to increased natural immunity owing to higher contact rate in densely populated areas.

It is challenging to define an ideal spatial window to focus on for investigating climate impact on meningitis dynamics: climate is a large-scale phenomenon; while it was proved in earlier studies that meningitis epidemics occur at a sub-district level [2,12,59,60]. However, the district scale is in our opinion the most appropriate to investigate periodic components: it is a large enough scale to detect periodic patterns for meningitis epidemics, while being small enough to capture spatial variability in dust and climate variables. Moreover, using this unusual scale to observe climate helped in highlighting a few phenomena. First, it was observed that RH variability between seasons decreases at the middle of the study period in the northern semi-desert part of Niger, which could be attributed to changes in climate with a possible expansion of the desert. Second, a six-month periodicity appeared in Wf and TEMP spectra. This is coherent with what we know of the climate in the area: (i) TEMP is driven by the solar intensity, with a negative impact of RH: it reaches its maximum in March in the core of the dry season, but another local maximum is reached at the end of the rainy season, in September; and (ii) Wf is the highest in the dry season when continental trade winds blow. However, the southern flux intensifies in July as the monsoon winds blow, with a consecutive increase in Wf (see the electronic supplementary material, figure S6). It is important to highlight these results, as up to now the climate and teleconnection researches in the Sahelian area mostly focused on the wet season. The dry season should equally be studied, for it is of major importance when relating climate to human health.

One limitation of this study concerns measurement errors and representativeness. First, owing to the high level of public awareness and concern, the degree of involvement of health professionals and the country-wide use of the WHO case definition [30], the reporting rate for meningitis cases is believed to be both high and consistent. Reporting error or delays are relatively unlikely, and should, however, affect data in a spatially and temporally consistent way. Second, climate estimates are obtained from reanalysis, which are the most representative estimates we can currently obtain, and are widely used by the climate research community [19,61–63]. Third, the AI representativeness has been tested: although it is perfectible, especially in terms of capturing the intensity of dust events in the dry season, it was proved to perform well in capturing the timing of those events [64–66]. As we focus in this study on variables' timing, results should not be affected. No other aerosol datasets covering such a long time period are available. Here, we provide an alternative to the issue of the appropriateness of measurements of dust captured over the whole atmospheric column when investigating dust impact on health: we aimed to correct DUST data from an altitude effect (which was assumed to be cyclic and consistent in the studied region) and approximate dust levels at the surface. The coherency in the results obtained using raw DUST data and corrected $DUST_C$ data, along with the length of the study period we are considering, strengthens our confidence in using these sets of data. Ideally, ground-level measurements of dust would be needed, but the existing ones are too sparse to be used in fine spatial scale studies such as this one (to our knowledge, in the region, we can locate no other station but the three of Sahelian Dust Transect). We hope for more stations to be setup in the future. Spatial dust data could also be obtained from simulation of dust emission and transport models such as CHIMERE [67,68]. Although current dust models were proved a good match with ground-level data at a large scale (monthly temporal scale), they still need to be tested at a smaller scale before being used in further studies [67–69].

To conclude, to our knowledge, this exploratory study is the first one (i) at a district level and weekly scale and (ii) to investigate and compare the link between the seasonality of meningitis versus dust and climate variables. We provide an important insight by defining dust loads as the prime parameter explaining the seasonality of meningitis. Up to now, few studies have investigated the impact of dust on health [70,71], and deplored a weak focus on West Africa. We provide here new evidence of this impact on meningitis in the given region. However, more quantitative studies are now needed to confirm and deepen our findings, to investigate the factors impacting the amplitude of the epidemics (including dust and climate), and to look for possible interaction effects. Finally, we would recommend the estimates of ground-level dust to be further improved. Ultimately, this refined knowledge of the dust impact on meningitis dynamic could help in improving the public health decision process.

A new conjugate vaccine against *Neisseria meningitidis* A is currently being introduced in the African Belt [72], and in the future will be used in preventive routine vaccination campaigns of infants. In the short- and long-term perspective, it is crucial to identify the determinants of the meningitis dynamics in order to be able to make epidemiological models more realistic and to test different scenarios of vaccination strategy. Wavelet analyses were used here to explore the complexity of environmental and epidemiological signals before the modelling stage [31]. The current epidemiological [73] and forecasting [74] models for meningitis considered so far a theoretical seasonality of the meningitis transmission dynamics. We now suggest integrating dust data in these models to make them more realistic and usable in a public health perspective.

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