A proposed methodology to estimate the cumulative life-time UVB exposure using geographic information systems: An application to multiple sclerosis

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Abstract

Background: The cause of multiple sclerosis (MS) is unknown; multiple risk factors have been implicated, including environmental exposures, such as sunlight. Many studies have relied on latitude alone as a crude proxy for sunlight exposure. We aimed to develop a protocol allowing a more detailed estimate of cumulative ambient ultra-violet B (UVB) exposure at critical time-periods over a patient’s life-course.

Methods: 4010 definite MS patients with a ‘movement history’ from birth to the study end (2005) were selected from the University of British Columbia, Canada’s MS Genetic database. Patient’s place of resident from birth were tracked, each place being geocoded (latitude and longitude) and assigned a UVB value using the NASA Total Ozone Mapping Spectrometer (TOMS) dataset. Combined, these data allowed an estimated UVB value for each patient based on year and location.

Results: Using this protocol, we provide a potentially more detailed cumulative UVB exposure for critical periods in a patients’ life history based on their individual spatial migration through time.

Conclusions: This protocol is intended to provide a framework for researchers to more accurately estimate UVB exposures for individuals over the course of their life history and may be useful for understanding etiology of MS and other chronic disease.

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1. Introduction

Multiple sclerosis (MS) is a chronic, degenerative disease of the central nervous system for which the exact etiology is not yet understood. Multiple risk factors may be involved including interactions between susceptibility genes and environmental factors (Milo and Kahana, 2010; Sospedra and Martin, 2005). Several clinical and epidemiological studies support the hypothesis that vitamin D levels - perhaps mediated by ultraviolet B exposure - are able to modulate disease processes in MS (Ascherio and Munger, 2007; Simon et al., 2011; van der Mei et al., 2011). Early papers reported that the frequency of MS was greater between 45 and 64 degrees latitude - than at lower latitudes (Kurtzke, 1977). These reports were organized geographically (Kurtzke, 1980) in a map that revealed bands of higher prevalence in Northern and Central Europe as well as North America and parts of Southern New Zealand and Australia (Kurtzke, 1980).

Assignations of latitude have been variously derived based on place of birth, location at puberty or place of symptom onset or diagnosis (Detels et al., 1978; Hammond et al., 2000; Sloka et al., 2008). There are two main shortcomings with latitude correlation to date. First, selecting single latitude for assignation of UVB exposure does not take into account the role of the entire life history and movements (e.g., what was the UVB exposure at key points in a patient’s history). Related to this is that the current methods are not able to account for increasingly mobile western populations (Beretich and Beretich, 2009). Second, latitude correlations do not measure actual ambient UVB exposure (i.e., the actual level of UV radiation reaching earth). Notable exceptions include recent use of satellite data to determine average UVB exposure at latitude (Beretich and Beretich, 2009; Sloka et al., 2008). Some have called for the calculation of more accurate population exposure estimates (Ebers, 2009), although to date, no standardized procedure has been developed. This paper introduces a method to calculate UVB exposure for patients at critical points as well as cumulative exposure over the course of their life history using widely available NASA data, with application to MS.

2. Methods

This was a retrospective study accessing patients with definite MS (Poser et al., 1983) or (McDonald et al., 2001) criteria) through the University of British Columbia (UBC) MS Clinic where detailed family histories are taken by a trained genetic counselor. From the “UBC MS Genetic database”, we identified MS patients with information detailing -their movement since birth to study end (2005) as well as the date (year) and location of each change in place of residency were collated. This was linked to UVB data obtained using the NASA Total Ozone Mapping Spectrometer (TOMS) data set. TOMS data consists of several data sets collected by NASA satellites during the period 1979 to 2005 (excluding 1994-95). Our study used TOMS’ Erythemal UVB data as it provides a record of UVB values reflected from the earth’s surface. This accounts for cloud coverage and only captures UVB that reaches earth. The raw data is collected and recorded daily by NASA and covers the world’s surface with 180 cells longitude, 288 cells latitude and a cell dimension of 1 x 1.25. The TOMS data UVB values consist of 3 digit values that required conversion (using a standard formula) in order to obtain the actual UVB value for each location. As the TOMS data did not provide UVB values for all locations within the study, a value of 999 (i.e., missing data) was assigned to areas without data.

In preparation for analysis, a UVB value was assigned to each year of each MS patient’s life. This value was calculated by averaging daily NASA values over the year (e.g. sum of all days/number of days of data). A UV reference table was developed providing a UVB value for each location for each year included in the study for each patient. The reference table served the purpose of allowing us to assign the correct UVB value to the ‘patient movement table’ based on time and location. To populate the table, all unique patients’ locations in the world were geocoded (approximately 2500 locations). Annual UVB surfaces were created for each year for which data were available. Days for which no data were recorded were then subtracted (i.e., 365 – days of no data). For years in which no UV data were recorded, averaged surfaces were created based on years for which data existed. Using the reference table, the correct UVB value could be assigned to each patient based on year and location.

Figure 1 illustrates the development of the patient movement table for assignation of a UVB value for each patient year since birth.

2.1. Data analyses

Geographic Information Systems (GIS) was the primary tool used to analyze and visualize the data. In order to ensure consistent projection within the software program, ArcGIS, the NASA surface cell dimensions of 1 x 1.25 were re-sampled at a cell dimension of 1 x 1 (ArcGIS only reads square cells). This required intermediary re-sampling with the raster application IDRISI so that cells could be imported into ArcGIS. After all the UVB surfaces were properly projected in ArcGIS, a reference table was created by overlaying the surfaces with the geocoded cities and extracting the UV value for each surface year. Figure 2.

3. Results

In total, 4010 definite MS patients were identified to have a movement history. As a group, they had resided in 2656 different localities for which a unique latitude, longitude and annualized UVB was assigned for every year of life. Of the patients in the database, 82% were born in Canada, 4.2% in the UK and 2.7% in the United States. Just over 10% were born elsewhere in the world. Most of these patients (87.1%) were of European ancestry and a breakdown of their ethnic backgrounds is given in Table 2. Other demographic or clinical information were not considered for this current methodological study.

Table 1 gives an example of cumulative UVB exposure at key points which might represent two patients’ lives (original details have been changed). The first patient, in red (ID 1), resided in locations with relatively low sun exposure. The second patient, in yellow (ID 2), lived in several locations,
one of which had significantly higher levels of sun exposure. As a result, for the patient in yellow, the total accumulative UVB exposure at age 15 was much higher. By comparison the latitude alone – which has commonly been used as a proxy for UVB exposure – gives little information. Slightly more information is provided using the NASA data for UVB for a token year for the latitude. However, a visual comparison between the cumulative UVB potential exposure value and the UVB potential exposure value for single latitude indicates clear differences.

The results from Table 1 provide a means of determining cumulative UVB exposure at critical points in each MS patient’s life. By contrast, latitude alone or even UVB for a token year at nominal latitude contain much less information – and are perhaps misleading given variations in sunlight at the places that share the same latitude and between different years. In Figure 3, we illustrate the difference in informational content for a hypothetical patient who was born and raised in each of the sample cities in a strip of latitude from 49° to 51° from Vancouver BC, Canada to the London, England. For each city (e.g., Vancouver, Calgary, Winnipeg and London), we calculated cumulative UVB exposure from 1980 to 2005. It is noteworthy that Calgary and London, while at the same approximate latitude, show very different values for UVB. Vancouver and Calgary, on the other hand are separated by two degrees of latitude and

Figure 1 Illustration of the protocol for UVB calculation with the resultant patient movement table that assigns an accumulated UVB value for each patient for each year since birth. This protocol enables researchers to accurately calculate potential UVB exposures for individuals—based on their specific geographical residences—over the course of their life history.

Figure 2 Illustrates the creation of the UV reference table by extracting the UVB value from each UVB surface for each unique location. Note: UVB values are for illustration purposes only.
yet have comparable figures. This variability points to a need to calculate values for individual locations rather than rely on latitude as a proxy.

Figure 4 provides a visualization of the lifetime cumulative UVB exposures of each MS patient in the database. Note that the majority live in British Columbia, Canada as might be expected, however, their trajectories from country of origin are also illustrated in the figure. Table 2.

Table 1 An example of two MS patients, with their respective moves and the cumulative UVB exposure at each move. In addition the accumulated UVB at critical time-points and for the year 2005 are also shown (grey row). By comparison, we show the relatively low informational value of latitude alone.

<table>
<thead>
<tr>
<th>ID</th>
<th>Move sequence</th>
<th>Year moved</th>
<th>City</th>
<th>Province</th>
<th>Country</th>
<th>Birth</th>
<th>Age</th>
<th>CumUV</th>
<th>Latitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1977</td>
<td>Port Hardy</td>
<td>British Columbia</td>
<td>Canada</td>
<td>Y</td>
<td>17</td>
<td>1361.3</td>
<td>50 41'N</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1994</td>
<td>Burns Lake</td>
<td>British Columbia</td>
<td>Canada</td>
<td>N</td>
<td>18</td>
<td>1433.9</td>
<td>54 1'N</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>1995</td>
<td>Vancouver</td>
<td>British Columbia</td>
<td>Canada</td>
<td>N</td>
<td>20</td>
<td>1599.6</td>
<td>49 23'N</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>1997</td>
<td>Victoria</td>
<td>British Columbia</td>
<td>Canada</td>
<td>N</td>
<td>28</td>
<td>2241.7</td>
<td>48 25'N</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1949</td>
<td>Vancouver</td>
<td>British Columbia</td>
<td>Canada</td>
<td>Y</td>
<td>24</td>
<td>2072.0</td>
<td>49 25'N</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1973</td>
<td>Winnipeg</td>
<td>Manitoba</td>
<td>Canada</td>
<td>N</td>
<td>28</td>
<td>2408.1</td>
<td>49 54'N</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1977</td>
<td>Calgary</td>
<td>Alberta</td>
<td>Canada</td>
<td>N</td>
<td>31</td>
<td>2644.7</td>
<td>51 1'N</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>1995</td>
<td>Vancouver</td>
<td>British Columbia</td>
<td>Canada</td>
<td>N</td>
<td>56</td>
<td>4792.4</td>
<td>49 13'N</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ID</th>
<th>UV birth</th>
<th>UV age</th>
<th>UV 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80</td>
<td>1205</td>
<td>2241.7</td>
</tr>
<tr>
<td>2</td>
<td>86</td>
<td>1295</td>
<td>4792.4</td>
</tr>
</tbody>
</table>

Figure 3 A two degree strip of latitude illustrating that latitude alone does not substitute for UVB exposure over a twenty-five year period.

4. Discussion

We demonstrate that it is possible to calculate geographically specific ambient UVB exposure values for patients. This is relevant particularly in the case of MS where several clinical and epidemiological studies support the hypothesis that ultraviolet B radiation (UVB) is able to modulate disease processes and risk in MS, perhaps through vitamin D (Ascherio and Munger, 2007; Milo and Kahana, 2010; Simon et al., 2011; van der Mei et al., 2011). Studies have included MS geographical distribution (Simpson et al., 2011), the relation between the month of birth and MS risk (Staples et al., 2010; Willer et al., 2004), the inverse association between ambient UVB and MS relapses (Tremlett et al., 2008) and lower levels of vitamin D during MS relapses (Simpson et al., 2010; Soilu-Hanninen et al., 2008).

The prevalence of MS has been shown to follow a north south gradient in its geographical distribution in several
countries (Simpson et al., 2011) such as the USA (Wallin et al., 2004), Australia (van der Mei et al., 2001) and some European countries including France (Vukusic et al., 2007) and Spain (Llorca et al., 2005). In these countries, the prevalence of MS increased with latitude with lower prevalence rates in the more equatorial regions, however, there are exceptions, notably Norway (Kampman and Brustad, 2008). Interestingly, in France and USA an inverse relation between MS prevalence and the minimum autumnal UV erythemal level was demonstrated.

In Newfoundland (Canada’s easternmost province), significant correlation was found between MS incidence and UVB radiation, and the risk of developing MS was mostly related to the geographical place of residence in the first year of life (Sloka et al., 2008). In Tasmania (Australia), lower risk of developing MS was associated with a higher sun exposure in the first 6-15 years of life (van der Mei et al., 2003). Interestingly, in France and USA an inverse relation between MS prevalence and the minimum autumnal UV erythemal level was demonstrated.

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Even the gestational environment might influence the risk of developing MS later in life; (Willer et al., 2004) (Staples et al., 2010) individuals born in the northern hemisphere in November had a lower risk of developing MS than those born in May (OR=1.19, 95%CI:1.14-1.25) (Willer et al., 2004) although this was only found in those with relapsing-onset MS, not primary-progressive (Sadovnick et al., 2007). The inverse has been observed in the southern hemisphere (Staples et al., 2010), with the greatest risk being those born in November-December compared to May-June (Staples et al., 2010).

Both UVB and vitamin D have been shown to modulate the immune system, primarily in animals (including the animal model of MS, experimental allergic encephalomyelitis (EAE), (Cantorna et al., 1996), but also in humans (Possonby et al., 2005; Smolders et al., 2008). Therefore, exposure to UVB has been implicated in the etiology of MS, either directly via its immunosuppressive effect or indirectly through vitamin D (Smolders et al., 2008) or perhaps melatonin synthesis (Constantinescu, 1995) all of which have immunomodulatory effects.

In this study, we do not examine the effects of UVB exposure on the etiology of MS. However, we provide an important first step towards more accurate analysis of these possible effects through the development of a preliminary protocol for calculating cumulative UVB exposure at critical points in patients’ life histories. This protocol is intended to provide an alternative to latitude based assumptions about UVB exposure (based on geographic location) as it uses daily UVB exposure to provide real potential cumulative exposure rather than exposure estimated based on latitude alone. In addition, it allows exposure to be calculated for key moments in patients’ life histories (e.g., birth, onset of puberty, onset of MS). This might be helpful in future research to help address how lifelong UVB accumulation affects MS. This protocol is generalizable across multiple disease studies where UVB exposure is considered a possible correlate and is fully adaptable to interrogate the importance of different UVB wavelengths or summer vs. winter UVB levels.

Limitations of our study include the inability to directly measure either actual sunlight exposure or serum vitamin D levels for each patient over their individual life course which would depend on a complex range of factors such as time spent outdoors, amount of skin exposed, skin colour and diet - such a study would likely be logistically impossible as well as prohibitively expensive. Nonetheless, cohort studies where a sub-set of patients are followed for finite periods of time would be useful to validate the association between ambient UVB and serum vitamin D across the seasons. Our study’s strength is its ability to provide geographically specific potential UVB exposure data - even as the patient moves through time and space during the course of their life.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Ethnic background of BC MS patients included in the study (n=4010).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnic background</td>
<td>N</td>
</tr>
<tr>
<td>European</td>
<td>3492</td>
</tr>
<tr>
<td>Asian</td>
<td>164</td>
</tr>
<tr>
<td>Othera</td>
<td>25</td>
</tr>
<tr>
<td>Mixed</td>
<td>220</td>
</tr>
<tr>
<td>Unknownb</td>
<td>109</td>
</tr>
<tr>
<td>Total</td>
<td>4010</td>
</tr>
</tbody>
</table>

aOther – African, Caribbean, First Nations, Central and South American.
bUnknown – 63 cases had known ethnicity either on the maternal or paternal side; 46 had unknown ethnicities on both sides.
5. Conclusion

Insufficient methodological data in previous studies has made replication of findings difficult, resulting in uncertainties. In particular, we suggest that individual latitudes cannot be assigned a universal UVB value; rather UVB is both spatially and temporally dynamic. As a result, UVB must be calculated on at least an annual basis for each location and for each patient throughout their lifetime. In combination, these two protocols result in cumulative lifetime UVB exposure data for each patient. We have developed a set of standardized protocols for the calculation of ambient UVB exposure over a lifetime - that takes into account patients’ geographical movement. We anticipate that the results will permit a standardized protocol for calculation of UVB exposure. Our research has important implications for ecological studies linking ambient UVB to incidence and prevalence and progression in MS and answers the calls of previous researchers for such a methodology (Beretich and Beretich, 2009; Ebers, 2009). We welcome discussion on refining these methods and encourage others to apply these methods in different geographical areas.

Conflict of interest

All other co-authors have no conflicts or disclosure to report.

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