Report

Autism prevalence in the United States with respect to solar UV-B doses: An ecological study

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Abstract:
Evidence is mounting that vitamin D deficiency is intimately involved in autism. We report on autism prevalence by US state for those aged 6–17 y in 2010 with respect to indices of solar UV-B (UVB) doses. We calculated autism prevalence rates for white, black and Asian Americans by using total prevalence and relative populations of minors for each ethnic group by state. Analyses omit AK and HI (considered extreme cases), WY (no data), along with AZ and ND for black Americans (low numbers) and DC, ME, MT, ND and SD for Asian Americans (low numbers). For white Americans, the regression coefficient for solar UVB doses and autism prevalence ranged from -0.52 in January to -0.57 in October. For black Americans, the regression coefficient for latitude was 0.61, whereas those for solar UVB ranged from -0.55 to -0.61. For Asian Americans, the values for solar UVB ranged from -0.28 to -0.38. The inverse correlation between solar UVB and autism prevalence is similar to that for many types of cancer in the US. The journal literature indicates that adverse effects on fetal brain development during pregnancy due to vitamin D deficiency can explain these findings. However, we cannot rule out a role of vitamin D deficiency in early life. These results add to the evidence that vitamin D deficiency may be an important risk factor for autism and suggest that pregnant women and autistic individuals raise their serum 25-hydroxyvitamin D concentrations above 30 ng/ml.

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Full Text

Introduction

Evidence is mounting that vitamin D deficiency is a risk factor for autism. Cannell[1] [2008] first proposed and later extended[2] [2010] the UV-B (UVB)-vitamin D-autism hypothesis. Kinney and co autism and vitamin D connection and suggested that "Vitamin D plays important roles in repairing DNA damage and protecting against oxidative stress—a key cause of DNA damage." Mostafa studied autistic children and found a strong correlation between better autism rating scales and higher 25(OH)D levels and between higher anti-neural antibodies and lower 25(OH)D levels.[4] Koi reviewed the evidence supporting this hypothesis and called for "urgent research" into vitamin D and autism. Despite the mounting evidence, the working hypothesis has not been accepted amo

A map of autism rates by state for children aged 6–17 y in the *Los Angeles Times* in December 2011[6] prompted this ecological study. The map showed highest rates in the Northeast and on t lowest among the Southern and Plains states. The trend of high rates in the Northeast and lowest rates in the Southern states is similar to that of many types of cancer,[7] which were linked to July.[8,9] Thus, we thought that the data, when analyzed in greater detail, might show an inverse correlation between solar UVB doses and prevalence of autism.

Results

Table 1 gives the regression results for solar UVB doses for several different months as well as latitude. For white and Asian Americans, the regression fits for UVB in March, July and Octobe stronger than those for UVB in January or latitude. However, for black Americans, the results for latitude were similar to those for UVB. The regression fits for black Americans were slightly stro Americans.

Table 1. Regression results, autism aged 6–17 y in the US in 2010 by state

Race, states	Factor	Linear fit (r, adjusted R^2, p)	Power law
White Americans (AK, HI, WY omitted)	UVB-vit D, Oct	-0.57, 0.31, *	0.60
	UVB-vit D Mar	-0.55, 0.29, *	0.58
	UVB Jul	-0.55, 0.28, *	0.57
	UVB-vit D, Jul	-0.54, 0.28, *	0.60
	UVB-vit D, Jan	-0.52, 0.25, *	0.52
	Latitude	0.48, 0.22, *	0.48

Black Americans (AK, AZ, HI, ND, WY omitted)	Latitude × latitude	0.63, 0.38, *	0.63
	Latitude	0.61, 0.36, *	0.63
	UVB-vit D, Oct	-0.61, 0.36, *	0.69
	UVB-vit D Mar	-0.59, 0.33, *	0.62
	UVB Jul	-0.57, 0.31, *	0.60
	UVB-vit D, Jan	-0.56, 0.31, *	0.65
	UVB-vit D, Jul	-0.55, 0.29, *	0.63
Asian Americans (AK, DC, HI, ME, MT, ND, SD, WY omitted)	UVB-vit D, Jul	-0.38, 0.13, 0.01	0.38
	UVB Jul	-0.36, 0.11, 0.02	0.35
	UVB-vit D, Oct	-0.32, 0.08, 0.04	0.33
	UVB-vit D Mar	-0.30, 0.07, 0.06	0.30
	Latitude × latitude	0.29, 0.06, 0.06	0.27
	Latitude	0.28, 0.05, 0.08	0.27
	UVB-vit D, Jan	-0.28, 0.05, 0.08	0.34

*

, $p < 0.001$; UVB-vit D, data for vitamin D production from UVB;[12] UVB Jul, data from reference **54**.

No significant correlations emerged for other possible risk-modifying factors such as air pollution, alcohol consumption, obesity, poverty, or smoking.

Figures 1–3 are scatter plots of the autism prevalence data with respect to solar UVB doses. **Figure 1** shows the results for white Americans with respect to October UVB vitamin D productio power-law fits to the data. **Figure 2** does the same for black Americans. **Figure 3** shows the results for Asian Americans with respect to July UVB vitamin D production. The linear regression ratios for low to high UVB of 2.4 for white Americans, 3.6 for black Americans and 1.7 for Asian Americans. In all three cases, prevalence of autism with respect to changes in solar UVB decre doses than at higher doses.

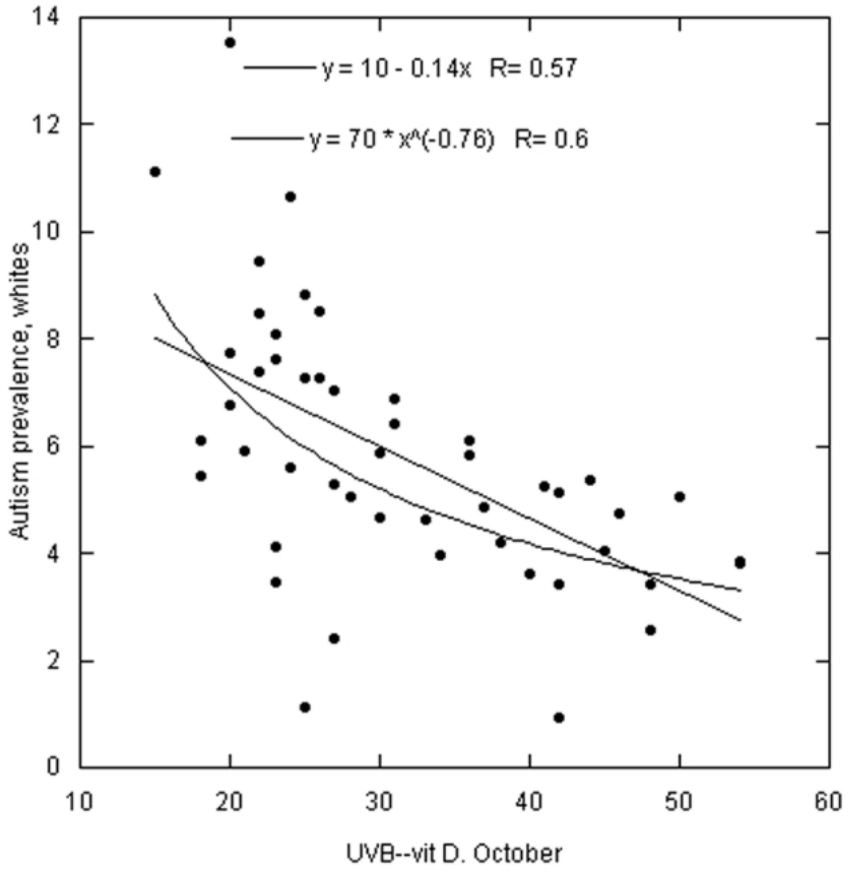

Figure 1. Scatter plot of autism prevalence for white Americans vs. solar UVB doses for October[13] with linear and power-law fits to the data. Prevalence data are in arbitrary units. Omitted s

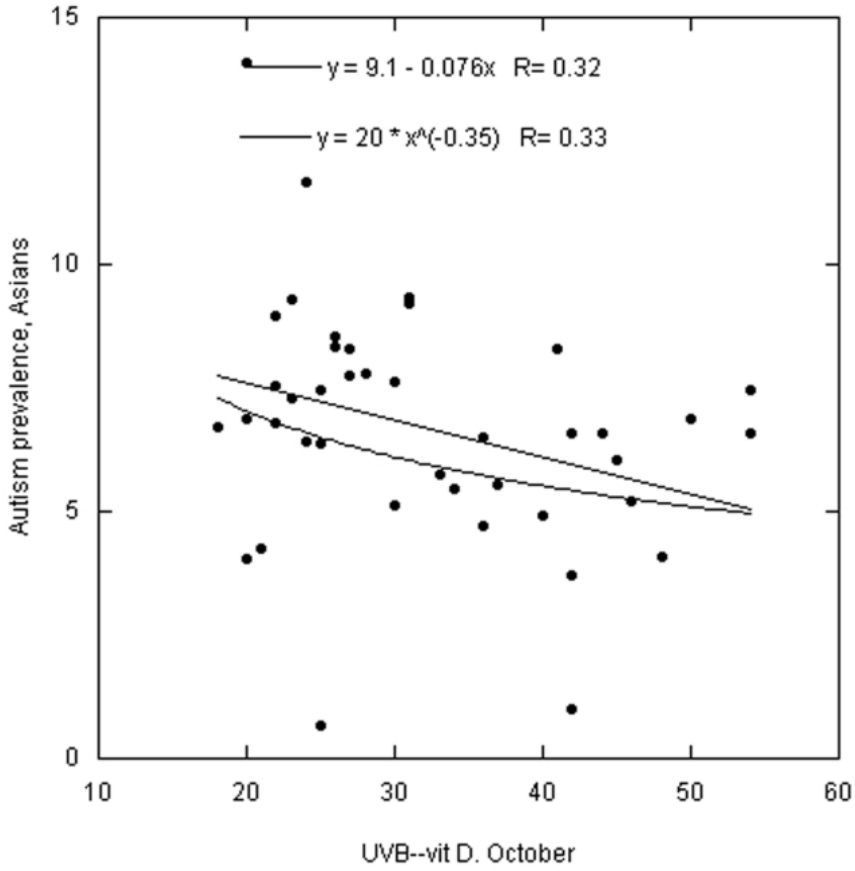

Figure 3. Same as **Figure 1** but for Asian Americans. Omitted states: AK, DC, HI, ME, MT, ND, SD and WY.

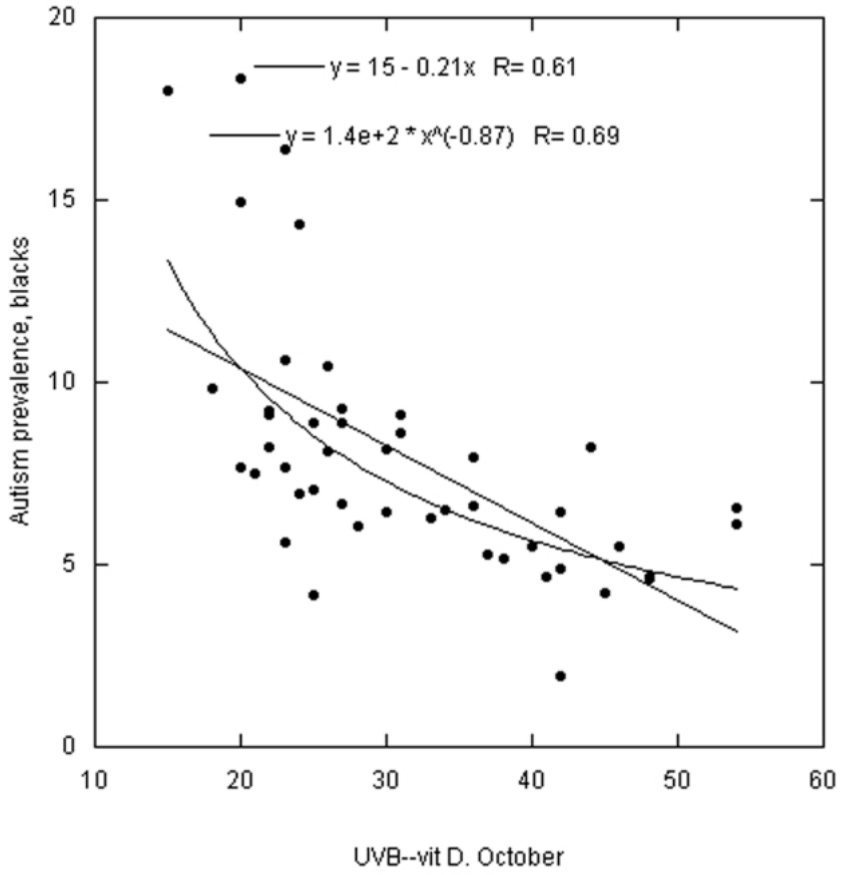

Figure 2. Same as **Figure 1** but for black Americans. Omitted states: AK, AZ, HI, ND and WY.

Discussion

The finding that, for both white and Asian Americans, solar UVB doses for March, July and October are much stronger than UVB doses in January or latitude suggests that vitamin D's effect is D production from solar UVB when doses are relatively high. This finding is similar to those for many types of cancer.[8,9] Other ecological studies directly correlated multiple sclerosis prevalenc The latitudinal dependence in the United States is considered an index of wintertime solar UVB doses[12] because summertime solar UVB doses are highly asymmetrical, being highest in the S the Northeast.[13] Low serum 25(OH)D concentrations in winter are associated with infectious diseases such as influenza,[14] which peaks in winter. However, for black Americans, the results for to those for UVB.

If we assume that solar UVB production of vitamin D is an important factor in reducing risk of autism, an important question is how vitamin D deficiency before and during pregnancy and in earl Reasonable evidence exists that autism is due in part to genetic factors. For example, evidence indicates that vitamin D status affects both male and female fertility,[15] which could be due to p the fetus. In addition, monozygotic twins are more likely to be concordant for autism than dizygotic twins.[16] Good evidence also exists that vitamin D deficiency during pregnancy leads to adve Maternal metabolic conditions during pregnancy (diabetes, hypertension and obesity) are associated with increased risk of offspring diagnosed with autism by age 5 y.[17] Vitamin D deficiency i diabetes,[18] and obesity is associated with lower serum 25(OH)D concentrations.[19] Animal model studies have documented adverse effects on fetal brain development for vitamin D-deficient mo prompted by an interest in schizophrenia, Sullivan and colleagues[21] associated family history of schizophrenia with increased risk of autism.

A study in Australia "found that the risk of women with vitamin D insufficiency (≤46 nmol/L) during pregnancy having a child with clinically significant language difficulties was increased close to women with vitamin D levels >70 nmol/L."[22] A study in the UK found that there were excess birth rates in April for several immune-mediated diseases found to be related to vitamin D deficiency providing evidence that vitamin D deficiency during fetal development is a risk factor for these diseases.[23]

Season of birth (or conception) affects risk of autism. In the 1980s and 1990s, excess birth rates for autism occurred around March.[24,25] However, Zerbo and colleagues[26] associated wintertim increased risk of autism. Maternal infection during pregnancy is associated with increased risk of autism,[3,27] as is elevated maternal temperature. See Edwards[29] for an explanation of how infe body temperature, is a risk factor for adverse birth outcomes.

Vitamin D reduces risk of both bacterial and viral infection.[30] Lower respiratory infections are relatively common during pregnancy.[31] Influenza infection during pregnancy is associated with incr schizophrenia in offspring.[32] Vitamin D may reduce the risk of influenza[32,33] as well as that of other acute respiratory infections.[34]

A study in Denmark found significantly increased risk of epilepsy for those born to mothers who experienced elevated temperature during pregnancy associated with infections.[35] Both epilepsy elevated birth rates in winter and lower birth rates in summer or fall.[24,36]

Although the journal literature supports the evidence for vitamin D deficiency before or during pregnancy as an important risk factor for autism, this ecological study cannot determine whether vi

plays a role although Mostafa and Al-Ayadhi's recent study indicates such a connection.[4] Both genetics and environment affect risk of autism.[16] However, separating genetic from environment

Since differences were found for those with different skin pigmentation, there might be some effects of solar irradiance other than vitamin D production involved in the link between solar UVB do autism. A number of papers have reviewed the neuroendocrinology of the skin.[38-41] For example, keratinocytes stimulated by UVR can produce and secrete a number of cytokines.[38] A recent with autism were "more likely to have decreased levels of both T helper-1(Th-1)-like cytokines (i.e. IFN-γ) and Th-2like cytokines (i.e. IL-4, IL-10)."[42] Since darker pigmentation reduces the effec keratinocytes, those with darker skin should produce fewer cytokines. Certainly more research is needed in this area.

UVA can increase serotonin production and reduce melatonin concentrations.[43] "Low maternal plasma serotonin may be a risk factor for autism through effects on fetal brain development.."[44] have a deficit of melatonin since supplementing them with melatonin improves sleep patterns.[45] Since dark skin reduces the production of serotonin and degradation of melatonin, those with lig decreased risk of autism and a recent review showed the opposite.[46] Obviously, more work needs to be done in this area.

There is some evidence that UVR contributed to regulation of the hypothalamic-pituitary-adrenal (HPA) axis and the inflammatory response system and that they may have systemic effects.[41] should increase the risk of autism and maternal stress during pregnancy is weakly associated with raised maternal cortisol.[47] Thus, more research is needed in this area.

Vitamin D recommendations

The Institute of Medicine determined that pregnant women require only 600 IU/d (15 μg/day) of vitamin D_3 (recommending the same for a 300-pound professional football lineman) and opine tha concentration of 20 ng/ml is adequate.[48] In the US, serum 25(OH)D concentrations during pregnancy are already low,[49,50] and black Americans have much lower serum 25(OH)D concentratio in general.[51] The optimal serum 25(OH)D concentration during pregnancy is above 30 ng/ml based on a number of observational studies. Representative studies reporting that levels above 30 n those related to pregnancy outcomes such as bacterial vaginosis,[52] birth weight,[53] primary Cesarean section delivery,[54] and pre-eclampsia.[55] In addition, gestational 25(OH)D concentrations normal fetal brain development[20,56] and levels above 30 ng/ml are associated with reduced risk of childhood neuropsychological impairments,[57] and development language difficulties.[58]

There is also evidence that serum 25(OH)D concentrations above 40 ng/ml might be considered optimal during pregnancy since optimal production of 1,25-dihydroxyvitamin D was achieved abo randomized controlled trial with pregnant women.[59,60] No adverse effects on calcium metabolism or other parameters were apparent in pregnant women taking 4000 IU/d of vitamin D_3.[60] A rece levels in women living a traditional life style near the equator found mean serum 25(OH)D levels of nearly 60 ng/ml in pregnancy, approximately triple that of pregnant women in more developed putatively live and work indoors.[61]

The optimum 25(OH)D levels for children with autism are unknown although Mostafa and Al-Ayadhi found a strong negative correlation between autism rating scales and 25(OH)D levels in child did not report a flattening of the association with higher vitamin D levels and improved autism scores although their study was limited by both the sample size and the low number of children wi They also found autistic children have lower 25(OH)D levels than do control children although both groups reported similar time outdoors.

Mean "natural" 25(OH)D levels (as opposed to "normal" 25(OH)D levels) are around 46 ng/ml, as recently discovered by Luxwolda et al. who studied 25(OH)D levels of hunter-gatherers in equato "natural" 25(OH)D levels were common among tanned lifeguards in Missouri.[63]

Conclusion

This ecological study finds that autism prevalence among those aged 6–17 y in 2010 was significantly inversely correlated with solar UVB doses. Taken together, these results and other findin vitamin D deficiency as an important risk factor for developing autism. Maternal vitamin D deficiency appears to play an important role although we cannot discount a role of vitamin D deficiency studies should evaluate the UVB-vitamin D-autism hypothesis in both pregnant women and children with autism.

Methods

WBG obtained prevalence data from the Data Accountability Center associated with the Individuals with Disabilities Education Act data. The numbers of children by state with autism in 2010 a Count (https://www.ideadata.org/PartBChildCount.asp (accessed Dec 16, 2011). Data used included the number of children with autism aged 6–17 y; those aged 6–21 y; and number of Asian, aged 6–21 y with autism. The data for those aged 6–17 y were not separated by race. WBG used the data by race for those aged 6–21 y with autism to estimate the number by race of those a

The data for total population aged 6–17 y by state are from Part C, Population and Enrollment Data, Table C-4, Number of and percentage change in estimated resident population ages 6–17, 2010 (https://www.ideadata.org/PopulationData.asp#2010 [accessed Dec 16, 2011]).

WBG calculated the estimated population by race and state for children aged 6–17 y, he calculated numbers of autism children for each race and state. WBG obtained racial populations by st y in 2009 from the US. Census Bureau (http://www.census.gov/compendia/statab/cats/population/estimates_and_projections_by_age_sex_raceethnicity.html [accessed Dec 18, 2011]). The fr were as follows: white (including Hispanics), 0.760; black, 0.151; and Asian, 0.043. WBG used these values to apportion the population by state into the three racial categories to calculate aut state.

The independent variables used in this ecological study were solar UVB doses and latitude. WBG used two sets of data for UVB doses. One was DNA-weighted surface UVB doses from the T Spectrometer (TOMS) for noon for July 1992.[64] Grant and Garland[9] used these data in an ecological study of cancer mortality rates. The other data set was monthly solar UVB doses weighted from TOMS, validated using ground-based measurements and averaged over the period 1980–1990 for 12:00–12:59 p.m. local time.[13] Solar UVB doses in the US in summer are highly asymm in the Southwest, lowest in the Northeast. The reasons for this asymmetry include that surface elevations are higher in the West, whereas stratospheric ozone column contents are lower. In a greater aerosol loading and cloud cover. For both sets of data, WBG estimated the UVB dose for each state from the maps in an effort to weight it by each state's population distribution. A pro from Fioletov and colleagues is that the contours are closely spaced in the Southwest, making this graphical approach less reliable for those states.

Latitude is an index for wintertime solar UVB dose and vitamin D production because solar zenith angle is much more important in winter than is surface elevation and stratospheric ozone colu latitude data to be near the center of population for each state. The second-order regression with latitude yielded the best model for multiple sclerosis prevalence among veterans of World War the US[10] Scientists have linked multiple sclerosis to the Epstein-Barr virus, and other diseases linked to this virus have peak rates in March.[65]

This report omits data for AK and HI because those states are at the extreme latitudes and were not used in other ecological studies such as those regarding solar UVB and cancer.[8] No data Wyoming. In addition, some states have few Asians and/or blacks with autism, yielding poor estimates of autism rates. For black Americans, analyses omitted AZ and ND. For Asian America SD were also omitted.

The analyses also used data for several possible risk-modifying factors, as has been done for cancer.[9] These factors included alcohol consumption, lung cancer mortality rates for females, obe population living below poverty level and particulate air pollution concentrations.

WBG conducted linear regression analyses with the SPSS 20.0 statistical package (IBM/SPSS, Chicago, IL) and power law regression analyses with KaleidaGraph version 4.02 (Synergy Soft Graphs were prepared using KaleidaGraph.

Disclosure of Potential Conflicts of Interest

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