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A review of prevalence studies of Autism Spectrum Disorder by latitude and solar irradiance impact

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A B S T R A C T

Autism Spectrum Disorder (ASD) is a lifelong disability with no known cause or cure. Among the suggested etiologies, is Cannell's hypothesis of a deficiency in Vitamin D the main natural source of which is Solar Ultraviolet-B (UVB) radiation. The aim in this paper is to build on this hypothesis and explore the relationship of solar irradiance of which UVB is a component, by latitude with the prevalence rates of ASD. Twenty-five reports published between 2011 and 2016 using comparable diagnostic criteria were reviewed. The results suggest a tendency for the prevalence rates of ASD to be lowest in countries near the equator and for this rate to increase as the latitude increases. These findings provide some support not just for the Vitamin D hypothesis, but also for a new proposition that along with UVB radiation, the entire solar radiation spectrum which reaches the earth, may play a role in ASD. While these results are both novel and encouraging in terms of the potential efficacy of exposure to natural sunlight, further research is warranted before results can be considered definitive, and before the implications of the findings can be implemented clinically.

Introduction

Autism Spectrum Disorder (ASD) is an umbrella term for multiple neurodevelopmental conditions characterized by repetitive or stereotyped behaviors and pervasive deficits in social communications and interactions [1]. ASD is considered a lifelong disability which has an impact on both the individual and the family [2,3], as well as being a cost to society in general [2,4]. Among these costs are additional health care, disability support in school and, in some instances, the loss of a productive working life and the provision of social security. In addition, ASD is associated with several comorbidities [5,6] such as Attention-Deficit/Hyperactivity Disorder [7–10], Obsessive Compulsive Disorder [7,8], anxiety disorders [11–15], sensory over-responsivity [13,16–19], sleep disorders [20–22], and gastrointestinal problems [13,20,23,24].

The prevalence of ASD, or at least reports thereof, have increased substantially from 1 in 500 in 1995, 1 in 250 in 2001 [25], to 1 in 68 in 2010 in the USA in children less than 8 years [26]. However, it is possible that rather than an actual increase in the rate of ASD, these statistics reflect higher prevalence associated with expanded definitions of ASD, increased public awareness and help-seeking. Further changes in the prevalence rates for ASD may also be a product of social destigmatization associated with ASD [27].

Despite the efforts of scientists who have investigated a myriad of environmental and genetic factors including air pollution [28–32]; environmental toxins such as mercury, nickel, selenium, lead, cadmium, aluminum, vinyl chloride and trichloroethylene [33–37]; genetic heritability [38–40]; hormonal imbalances such as oxytocin [41], vasopressin [42], and more recently Vitamin D deficiency [43,44] the etiology of ASD remains uncertain.

Following Cannell's proposal [43,44] that Vitamin D deficiency could be a risk factor for ASD several researchers have found low Vitamin D levels in patients with ASD [45,46], their siblings [47] and also maternal deficiencies [4,48,49]. Laboratory research has explored the genes regulated by Vitamin D [50,51]. Overall, these results have pointed towards an association between Vitamin D deficiency and autism-related traits [44,52]. Further support for Cannell's hypothesis comes from reports that some level of improvement in autistic symptoms has been achieved via the administration of Vitamin D supplements [53–55]. Despite this tentative support for an association between Vitamin D and ASD, no conclusive evidence of this relationship

Abbreviations: ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; ASSQ, Autism Spectrum Screening Questionnaire; ASQ, Autism Screening Questionnaires; BSA, Body Surface Area; CAST, Mandarin Childhood Autism Spectrum Test; ICD-10, International Classification of Diseases, 10th edition; ISAA, Indian Scale for Assessment of Autism; M-CHAT, Modified Checklist for Autism in Toddlers; M-CHAT/ES, Spanish version of the Modified Checklist for Autism in Toddlers; VBAS, Vineland Adaptive Behaviour Scale

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has emerged.

In line with the research into Vitamin D deficiency, recent research has addressed a link between solar irradiance and ASD [56–58]. Solar irradiance is the measure of the sun's electromagnetic spectrum over all wavelengths per unit area, usually described in watts per meter^2 (W/m^2) units [59]. The earth's atmosphere filters the sun's electromagnetic radiations leaving Ultraviolet (UV), Visible, and Infrared radiations as the main biogenically relevant components [60] to reach the earth's surface. UV is further classified into UVA, UVB and UVC [59,61]. UVA reaches the earth's surface throughout the year, UVB reaches the surface only when the sun is high in the sky, while UVC is completely blocked by the earth's atmosphere [59].

When people are exposed to UVB radiation, 7-dehydrocholesterol present in the skin is converted to pre-Vitamin D_3 and provides the main source of natural Vitamin D to the body [56] Some research has reported a correlation between low solar UVB and high ASD prevalence [56–58] with this higher ASD prevalence attributed to lower levels of sunlight based Vitamin D production. These studies were, however, limited in scope. Firstly, they focused only on the UVB based Vitamin D part of the electromagnetic spectrum; secondly, there was a noticeable omission of ASD prevalence rates from countries near the equator, which receive the highest levels of solar irradiance.

The aim of current study was to build on these investigations by examining the incidence of ASD across the globe by latitude and its relationship with solar irradiance which decreases as distance from the equator increases. This study, for the first time, proposes a link between ASD and solar irradiance across all electromagnetic wavelengths. This hypothesis will be investigated by comparing the results of published epidemiological studies from different countries and plotting their ASD prevalence rates by the latitude of the data sources.

Method

Published data were used for this study therefore approval from the University's Ethics Committee was not required.

Inclusion Criteria. Reports on the prevalence of ASD in children and adolescents were sought via searches of the major databases (PubMed, Google Scholar, ScienceDirect, Medline, Psychinfo) and a non-content database (Web of Knowledge). Search terms of "Autism" and "incidence/prevalence/epidemiology" were used. Subsequent searches included the name of countries/regions where gaps in geographical areas were identified. In order to minimize the impact of any unknown factors and diversity in earlier assessments, only the latest reports based on comparable diagnostic criteria were reviewed for this study.

Each study revealed by the search was examined individually and included in the analysis if it met the following criteria: 1) Original publication between 2011 and 2016; 2) reported on samples less than 18 years of age; 3) used recognized diagnostic criteria (e.g. DSM-IV or ICD-10) or nationally modified diagnostic criteria for determining the prevalence of ASD; 4) was representative of a reasonably defined geographic area, that is, inside 10 degrees of latitude (for determination of latitude and solar irradiance levels); and 5) represents the largest sample size.

In sum 25 studies met all four inclusion criteria. A further study from Australia that did not meet the inclusion criteria due to its wide geographical coverage exceeding 10 degrees of latitude will be discussed separately.

Results and discussion

The locations of the 25 studies reviewed are identified on the map in Fig. 1. Although prevalence rates from some regions that is, Russia and southern Africa, are not represented, with respect to street level solar irradiance at latitudes, the entire globe is represented (Fig. 1). An overview of the studies is listed in Table 1 including sample age, ASD prevalence and the diagnostic criteria used. The prevalence rates plotted by their respective latitude and solar irradiance level [62] are shown in Fig. 2.

Cannell's hypothesis [43], wherein he linked low levels of Vitamin D with ASD, was explored with respect to solar irradiation as a natural source of Vitamin D, and the results provide partial support for the exploration of this relationship. In general, the prevalence of ASD is shown to increase with increasing latitude while decreasing with increasing altitude. Fluctuations in both factors may be attributable to differences in elevation, pollution levels, annual solar irradiance, individual Body Surface Area (BSA) exposure, use of sunscreen protections, and skin pigmentation.

Overall, there is a tendency for ASD prevalence rates to increase and solar irradiance to decrease as the distance from the equator increases is shown in Fig. 2. There are peaks in prevalence rates which diverge from the line of best fit with Japan, South Korea and China having considerably higher prevalence rates of ASD while France has a lower rate (Table 1).

A notable finding is the increase in ASD prevalence above 25° latitude which maybe attributable to the decrease in solar irradiance which, until that point shows only a minor decrease. The other main finding is the continual increase of ASD prevalence above 33° latitude. During the winter months for those living above approximately 33° latitude very little if any Vitamin D_3 can be produced in the skin from sun exposure [87] due to an increase in blockage of UVB by the atmosphere. Support for this premise can be seen in reports from Boston, USA (42 °N), Edmonton, Canada (52 °N), and Bergen, Norway (61 °N) where residents are reported to be unable to produce sufficient quantities of Vitamin D in their skin for four, five, and six months of the year, respectively [87,88]. Similar findings have been reported elsewhere [89–91].

In the reports reviewed, Oman [69] has the lowest prevalence of ASD followed by Taif, Saudi Arabia [67], Costa Rica [64], Himachal Pradesh, India [73], Quito, Ecuador [63], Leon, Mexico [66], Atibaia, Brazil [68], Taiwan [70] and Shoranur, India [65] in that order. All of these regions lie below 25° latitude except for Himachal Pradesh (India) and the prevalence rates were all less than 0.31%.

The Oman study was based on the nation-wide coverage of participants diagnosed at one center. From 798,913 children aged 0–14 years only 113 cases of ASD were found based on DSM-IV-TR criteria. In addition to being close to the equator, Oman has a hot desert climate. Both of these may play a role in higher exposure to solar irradiance. The study from Saudi Arabia shows a prevalence rate of 0.035% from a sample population of 22,950 7–12 year-old students in the primary schools of Taif district. The Costa Rican study was based also on a nation-wide sample [92,93] where, in the 1–5 year-old population, the prevalence of ASD was 118 children from a sample size of 290,375. The Himachal Pradesh study was carried out at 32° latitude in the Himalayan Mountains in India and the only study beyond 25° latitude to have a prevalence rate of less than 0.3%. The reported low prevalence rate of 0.09% may be attributed to the elevation at which this study was carried out as at high elevation, solar irradiance (including UVB) is higher than at sea-level due to reduced travel-distance through the earth's atmosphere. Lower ASD prevalence at higher elevation further supports the argument for its association with solar irradiance.

In the Indian study [73] 11,000 children aged 1–10 years in the identified region were surveyed by trained investigators using a Hindi language version of the Indian Scale for Assessment of Autism (ISAA) based on the Childhood Autism Rating Scale (CARS). The authors of the Ecuadorian study [63] reported a prevalence rate of 0.11% in school going children of 5–15 years. The Leon (Mexico) study also found a low prevalence of 0.11% [66]. This Mexican study has reported on ASD rates in mainstream school going children and special education school children. The former prevalence rate was included here as a better representation of the overall population sample. Paula et al. [68] looked

Fig. 1. Red dots depicting the location of prevalence studies. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Worldwide reports of prevalence of ASD (%) by latitude [46,63–86].

Latitude	Region	Age	%	Sample Size	Criteria	Ref
00°14′	Quito, Ecuador	5–15	0.11	51,453	DSM-III, DSM-IV	[63]
8–10 °	Costa Rica	1–5	0.05	290,335	M-CHAT, VBAS	[64]
10°77′	Shoranur, India	1–15	0.31	8362	DSM-IV-TR	[65]
21°07′	Leon, Mexico	8	0.11	4431	DSM-IV-TR	[66]
21°26′	Taif, Saudi Arabia	7–12	0.04	22,950	AASQ	[67]
23°07′	Atibaia, Brazil	7–12	0.27	10,503	ASQ	[68]
17–24°	Oman	0–14	0.01	798,913	DSM-IV-TR	[69]
22–25°	Taiwan	0–17	0.29	372,642	ICD-9	[70]
28°9′	Las Palmas, Canary Islands	1–3	0.61	1796	M-CHAT/ES	[71]
29–33°	Israel	8	0.49	2,431,649	DSM-IV-TR	[72]
32°26′	Himachal Pradesh, India	< 11	0.09	11,000	ISAA	[73]
32°54′	Tripoli, Libya	1–10	0.31	38,508	DSM-IV	[74]
33–35°	Fukuoka-Tokyo, Japan	3	2.54	2516	DSM-IV-TR	[75]
33°53′	Beirut, Lebanon	1–4	1.5	998	M-CHAT	[76]
34°03′	LA County, USA	3–5	0.46	1,626,354	DSM-IV-R	[77]
37°34′	Goyang, South Korea	7–12	2.64	55,266	ASSQ	[78]
39°55′	Beijing, China	6–10	1.19	737	CAST	[79]
40°45′	Utah, USA	4,6,8	0.65	226,391	DSM-IV	[80]
43°25′	Haute-Garonne, France	7	0.37	307,751	ICD-10	[81]
49–59°	Manitoba, Canada	0–14	1	307,900	ICD-9, ICD-10	[82]
53°18′	South Dublin, Ireland	6–11	1.15	5457	EPAP	[83]
55°-60°	Scotland, United Kingdom	4–18	1.6	684,415	ICD-10, DSM-V	[84]
59°19′	Stockholm, Sweden	0–17	1.44	495,864	DSM-IV, ICD-10	[85]
62°00′	Faroe Islands	7–16	0.94	7128	DISCO-11	[46]
63–66°	Iceland	11–15	1.2	22,229	ADI-R or ADOS	[86]

at ASD prevalence in a less urbanized region of Atibaia (Brazil). Their finding was an ASD prevalence of 0.27%. The report from Taiwan is based on a sample of 372,642 aged younger than 18 years [70]. The cumulative prevalence of ASD was found to be 0.287%. The other Indian study is from a semi-urban Indian region and reported a prevalence of 0.3% for 1–15 years old age-group [65]. Overall, the reported prevalence rates of these studies strengthen the findings with respect to the current interpretation of the data.

The rest of the studies show a continuous rise in the ASD prevalence corresponding to their increasing latitudes. In view of the fact that there is reduced UVB during the winter season above 33° latitude, an increasing trend beyond this latitude may indicate that the entire solar irradiance spectrum has a role in the ASD prevalence, otherwise, there would have been more or less uniform rates beyond 33° latitude.

In the regions above 33° latitude the peaks of Japan, South Korea and China diverge from the line of best fit, having considerably higher prevalence rates of ASD while France has the lowest rate. South Korea has the highest prevalence in the reports reviewed in this study. The target population in that report included all children 7–12 years old (N = 55,266) in the Ilsan district of Goyang City near Seoul in South Korea [78]. Autism Spectrum Screening Questionnaire (ASSQ) was used and a prevalence of 2.64% was found. Data from two prospective community cohorts, namely Fukuoka Cohort and Tokyo Cohort were used in the study from Japan [75]. Fukuoka Cohort comprised 1851 children and Tokyo Cohort comprised 665 children with 51 and 13 of them being confirmed as having ASD, respectively, using DSM-IV-TR. The prevalence rate across the combined samples was 2.54%. In the Chinese study, the Mandarin Childhood Autism Spectrum Test (CAST) was used with 737 pupils aged 6–11 in two mainstream primary schools in Xicheng District in Beijing [79]. The prevalence rate was 1.19%. If low solar irradiance reaching the street level due to high pollution and smog levels in Beijing is considered, the high prevalence may be explained. South Korea and Japan do not have such high levels of pollution, yet their ASD prevalence rates are the highest in the reports reviewed. Weather might play a role, such as the longer and harsher winters experienced in these regions which lead to less BSA exposure or longer rainy seasons with cloud cover over 5.5 octa [94] which would further reduce UVB exposure days. The additional clothing required to keep warm in these harsher climates reduces the skin area exposed to sunlight, and may reduce vitamin D levels [95], however, this and other conjectures need to be investigated before drawing any conclusions.

It is important that future studies heed these factors in order to accurately judge the likely impact of solar irradiance on ASD. Since these countries are generally populated by the same race, it might also be that their race is more susceptible to ASD than the rest. This suggestion would need to be studied in comparison with Taiwan's ASD prevalence which is much lower (0.287%) at 25° latitude [70]. Its subtropical climate with year-round high solar irradiance is also important to consider in future comparative studies.

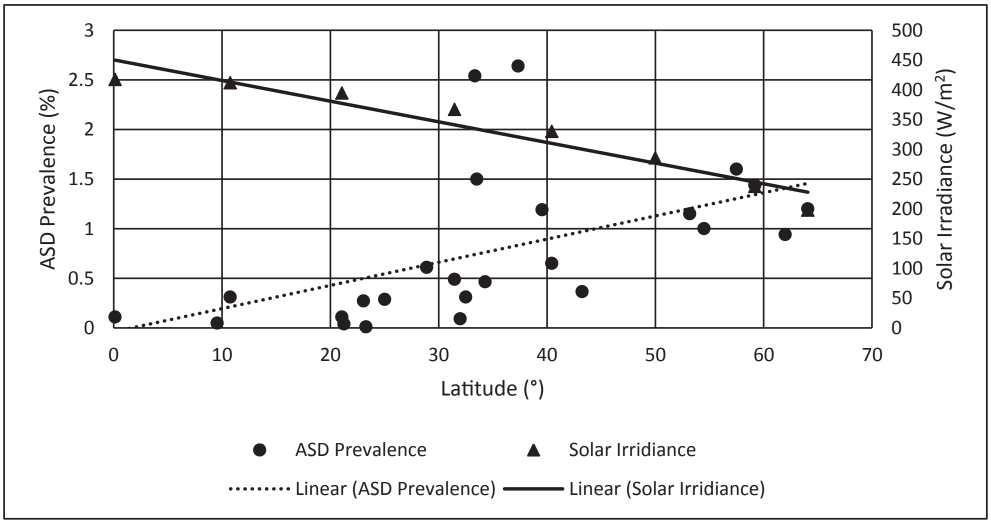

Fig. 2. ASD prevalence and solar irradiance by latitude.

The other noticeable exception from the increasing trend line is Haute-Garonne in France at 43° latitude. It has lowest prevalence of 0.365% [81] in regions above 33° latitude. This low rate merits further exploration and may relate to these children engaging more in outdoor activities and the local climatic/geographic factors. While van Bakel et al. [81] cited ICD-10 as the diagnostic criteria used to assess prevalence of ASD their figures were drawn from a French area data base. This database itself may have contained inaccuracies or, of some concern, is Danielle Langloys' (the Presidente of Austisme France) suggestion that France in general lacks appropriate diagnostic criteria for ASD and its incidence is underrated.

The five studies from northern Europe are from above 50° latitude. All of them have a prevalence rate of 1% or higher with Faroe Island having the lowest rate followed by South Dublin (Ireland), Iceland, Scotland (United Kingdom) and Stockholm (Sweden) in that order. Faroe Island study [45] revealed a prevalence rate of 0.94% from all 7–16 year-olds living on the island who were followed up till the age of 15–24 [46]. The report from South Dublin was based on the new European Protocol for Autism Prevalence (EPAP) for ASD prevalence measurement [83]. The authors reported a prevalence rate of 1.15% in 6 to 11-year-olds in a sample size of 5,457. The Icelandic study is based on a nation-wide database of ASD children aged 11–15. A total of 267 children were diagnosed with ASD from 22,229 children recorded in the birth cohort with a prevalence rate of 1.2% [86]. The investigation from Stockholm (Sweden) reported a prevalence of 1.44% in 0–17 year-olds [85]. A total of 7121 children were diagnosed with ASD in a cohort of 495,864 using DSM-IV until 2008, and ICD-10 since 2009. The Scottish study reported a prevalence rate of 1.6% [84] based on data from the annual Scottish Pupil Census which covers all publicly funded primary, secondary and special schools, some 684,415 students aged 4–18 [96]. In the UK ICD-10 and DSM-V are used as the main diagnostic criteria for ASD [97].

Overall, countries nearer the equator that is, below 25° latitude, the approximate latitude of the Tropics of Capricorn and Cancer, have prevalence rates below 0.35% while the European and North American countries have reported rates above 0.35%. This contrast in prevalence rates which we propose is linked to exposure to solar irradiance merits further investigation.

Study limitations and future work

A comprehensive review of the published literature was conducted to establish a global picture of ASD prevalence rates across different latitudes. However, prevalence studies give only a cross-sectional view of the number of the people suffering a disease at a specific point in time. Although attempts were made to use comparable criteria, there is always a challenge in comparing prevalence studies from different regions, with differences in case definitions, case identification (or case ascertainment), and case evaluation methods. The range of diagnostic criteria used, albeit internationally recognized, pose another challenge to ideal comparisons. Ideally, one criterion is needed to get an accurate picture of the change in ASD prevalence. Additionally, solar irradiation and hence sun exposure and more particularly Vitamin D levels, had to be inferred based on the reported location of the study but it is possible that those living near the equator could avoid the sun while those at higher latitudes might take advantage of all available daylight.

Small sample sizes in some studies is another weakness as is the diversity in the ages of the children assessed. Due to the remote locations of some studies from developing countries, there is a high probability of the sample having an overall similar genepool so that if a specific genepool has a low or high ASD susceptibility, this would distort the results. This proposition then raises questions about the impact genes have on ASD prevalence, as for instance, the studies of Chinese samples reveal the highest rates of ASD which gives some credence to this factor for future studies. It is highly probable that children in colder climates remain indoors more where poorer air quality [98] and possibly more time spent watching television [99,100] may contribute to, or compound the effects of lack of vitamin D_3, in the onset of ASD.

Universal healthcare systems in some developed countries like that of Japan, Australia and United Kingdom posed their own constraints. Due to the availability of national databases of children with ASD, small regional prevalence studies are scarce in such countries. Lastly, there is a shortage of ASD studies from countries below 20 ° latitude. These two factors pose further barriers to any similar study.

An accurate assessment of ASD prevalence with respect to solar irradiance necessitates studies across a range of latitudes from small regions. All of the above highlighted limitations may be overcome if a study were undertaken in Australian cities. Australia is the only country in the world that stretches from 10°S to over 45 °S latitude providing year-round maximum solar irradiance in its north to the minimum irradiance in the south within one political and medical systems. While Bent et al. [101] reported ASD prevalence rates in Australia, this was by state each of which stretch over several degrees of latitude. Even so, the Northern Territory (approximately 11° to 25°S) had the lowest reported ASD rate of 0.376% and Tasmania (approximately 41° to 45°S) had 0.752%. This change between two Australian states strengthens the argument that solar irradiance has an impact on ASD.

Conclusion

In this review, the aim was to explore the link between solar irradiance and the prevalence of ASD. This study for the first time has shown, theoretically, a relationship between low solar irradiance and ASD, particularly noted by the low rates in countries near the equator and Northern Territory (Australia) and high rates in Europe and Tasmania (Australia). The results of this review provide some support for Cannell's hypothesis [43,44] that lack of vitamin D, which in its natural form comes from exposure to UVB in sunlight, is implicated in ASD.

In conclusion, the findings of this review add support to the hypothesis that lack of exposure to full spectrum of solar irradiance increases the rate of ASD prevalence. These finding may contribute to understanding the etiology and pathogenesis of ASD. It might also be that exposure to sunlight might be an inexpensive and effective intervention technique in prevention or to reduce the impact of ASD on the child and family. Further studies are required to support this hypothesis.

Conflict of interest

The authors have no conflicts of interest associated with this paper.

References

[1] A. P. Association, Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub, 2013.
[2] Lavelle TA, Weinstein MC, Newhouse JP, Munir K, Kuhlthau KA, Prosser LA. Economic burden of childhood autism spectrum disorders. Pediatrics 2014;133(3):e520–9.
[3] Y. Kamio, N. Inada, Early diagnosis of ASD in toddlers and school children: community studies and national surveys in Japan. In: Comprehensive guide to autism, Springer, 2014, pp. 2561–2577.
[4] Magnusson C, et al. Maternal vitamin D deficiency and the risk of autism spectrum disorders: population-based study. Br J Psychiatry Open 2016;2(2):170–2.
[5] Mannion A, Leader G. Comorbidity in autism spectrum disorder: a literature review. Res Autism Spectrum Disord 2013;7(12):1595–616.
[6] Frye RE, Rossignol DA. Identification and treatment of pathophysiological comorbidities of autism spectrum disorder to achieve optimal outcomes. Clin Med Insights Pediatr 2016;10:43.
[7] Leyfer OT, et al. Comorbid psychiatric disorders in children with autism: interview development and rates of disorders. J Autism Dev Disord 2006;36(7):849–61.
[8] van der Plas E, Dupuis A, Arnold P, Crosbie J, Schachar R. Association of autism spectrum disorder with obsessive-compulsive and attention-deficit/hyperactivity traits and response inhibition in a community sample. J Autism Dev Disord 2016;46(9):3115–25.
[9] Visser JC, Rommelse NN, Greven CU, Buitelaar JK. Autism spectrum disorder and attention-deficit/hyperactivity disorder in early childhood: a review of unique and shared characteristics and developmental antecedents. Neurosci Biobehav Rev 2016;65:229–63.
[10] Hartman CA, Geurts HM, Franke B, Buitelaar JK, Rommelse NN. Changing ASD-ADHD symptom co-occurrence across the lifespan with adolescence as crucial time window: illustrating the need to go beyond childhood. Neurosci Biobehav Rev 2016;71:529–41.
[11] White SW, Oswald D, Ollendick T, Scahill L. Anxiety in children and adolescents with autism spectrum disorders. Clin Psychol Rev 2009;29(3):216–29.
[12] van Steensel FJ, Bögels SM, Perrin S. Anxiety disorders in children and adolescents with autistic spectrum disorders: a meta-analysis. Clin Child Fam Psychol Rev 2011;14(3):302.
[13] Mazurek MO, et al. Anxiety, sensory over-responsivity, and gastrointestinal problems in children with autism spectrum disorders. J Abnorm Child Psychol 2013;41(1):165–76.
[14] Vasa RA, et al. Age-related differences in the prevalence and correlates of anxiety in youth with autism spectrum disorders. Res Autism Spectrum Disord 2013;7(11):1358–69.
[15] Williams S, Leader G, Mannion A, Chen J. An investigation of anxiety in children and adolescents with autism spectrum disorder. Res Autism Spectrum Disord 2015;10:30–40.
[16] Green SA, Ben-Sasson A. Anxiety disorders and sensory over-responsivity in children with autism spectrum disorders: is there a causal relationship? J Autism Dev Disord 2010;40(12):1495–504.
[17] Green SA, et al. Overreactive brain responses to sensory stimuli in youth with autism spectrum disorders. J Am Acad Child Adolesc Psychiatry 2013;52(11):1158–72.
[18] Schauder KB, Bennetto L. Toward an interdisciplinary understanding of sensory dysfunction in autism spectrum disorder: an integration of the neural and symptom literatures. Front Neurosci 2016;10.
[19] Marco EJ, Hinkley LB, Hill SS, Nagarajan SS. Sensory processing in autism: a review of neurophysiologic findings. Nature Publishing Group; 2011.
[20] Klukowski M, Wasilewska J, Lebensztejn D. Sleep and gastrointestinal disturbances in autism spectrum disorder in children. Dev Period Med 2015;19(2):157–61.
[21] Rossignol DA, Frye RE. Melatonin in autism spectrum disorders: a systematic review and meta-analysis. Dev Med Child Neurol 2011;53(9):783–92.
[22] S. Miano, F. Giannotti, F. Cortesi, Sleep disorders and autism spectrum disorder. In: Psychiatric Symptoms and Comorbidities in Autism Spectrum Disorder: Springer, 2016, pp. 111–128.
[23] Mayer EA, Padua D, Tillisch K. Altered brain-gut axis in autism: comorbidity or causative mechanisms? BioEssays 2014;36(10):933–9.
[24] C. S. Rosenfeld, Microbiome disturbances and autism spectrum disorders, Drug Metabolism and Disposition, p. dmd. 115.063826, 2015.
[25] Weintraub K. Autism counts. Nature 2011;479(7371):22.
[26] M. Wingate et al., Prevalence of autism spectrum disorder among children aged 8 years-autism and developmental disabilities monitoring network, 11 sites, United States, 2010, MMWR surveillance summaries, vol. 63, no. 2, 2014.
[27] Liu KY, King M, Bearman P. Social influence and the Autism epidemic. Am J Sociol 2010;115(5):1387–434.
[28] Windham GC, Zhang L, Gunier R, Croen LA, Grether JK. Autism spectrum disorders in relation to distribution of hazardous air pollutants in the San Francisco Bay area. Environ Health Perspect 2006:1438–44.
[29] Becerra TA, Wilhelm M, Olsen J, Cockburn M, Ritz B. Ambient air pollution and autism in Los Angeles county, California. Environ Health Perspect (Online) 2013;121(3):380.
[30] A.E. Kalkbrenner, J.L. Daniels, J.-C. Chen, C. Poole, M. Emch, J. Morrissey, Perinatal exposure to hazardous air pollutants and autism spectrum disorders at age 8, Epidemiology (Cambridge, Mass.), vol. 21, no. 5, p. 631, 2010.
[31] Volk HE, Hertz-Picciotto I, Delwiche L, Lurmann F, McConnell R. Residential proximity to freeways and autism in the CHARGE study. Environ Health Perspect 2011;119(6):873.
[32] Volk HE, Lurmann F, Penfold B, Hertz-Picciotto I, McConnell R. Traffic-related air pollution, particulate matter, and autism. JAMA Psychiatry 2013;70(1):71–7.
[33] Felicetti T. Parents of autistic children: some notes on a chemical connection. Milieu Therapy 1981;1:13–6.
[34] Kinney DK, Barch DH, Chayka B, Napoleon S, Munir KM. Environmental risk factors for autism: do they help cause de novo genetic mutations that contribute to the disorder? Med Hypotheses 2010;74(1):102–6.
[35] Al-Farsi YM, et al. Levels of heavy metals and essential minerals in hair samples of children with autism in Oman: a case–control study. Biol Trace Elem Res 2013;151(2):181–6.
[36] Blaurock-Busch E, Amin OR, Dessoki HH, Rabah T. Toxic metals and essential elements in hair and severity of symptoms among children with autism. Maedica 2012;7:38.
[37] Geier DA, Kern JK, King PG, Sykes LK, Geier MR. Hair toxic metal concentrations and autism spectrum disorder severity in young children. Int J Environ Res Public Health 2012;9(12):4486–97.
[38] Frazier TW, et al. A twin study of heritable and shared environmental contributions to autism. J Autism Dev Disord 2014;44(8):2013–25.
[39] Sandin S, Lichtenstein P, Kuja-Halkola R, Larsson H, Hultman CM, Reichenberg A. The familial risk of autism. JAMA 2014;311(17):1770–7.
[40] Heil KM, Schaaf CP. The genetics of autism spectrum disorders–a guide for clinicians. Curr Psychiatry Rep 2013;15(1):334.
[41] Anagnostou E, et al. Intranasal oxytocin versus placebo in the treatment of adults with autism spectrum disorders: a randomized controlled trial. Mol Autism 2012;3(1):16.
[42] Carson DS, et al. Arginine vasopressin is a blood-based biomarker of social functioning in children with autism. PLoS ONE 2015;10(7):e0132224.
[43] Cannell JJ. Autism and vitamin D. Med Hypotheses 2008;70(4):750–9.
[44] Cannell JJ. Vitamin D and autism, what's new? Rev Endocr Metabol Disord 2017;18(2):183–93.
[45] Wang T, et al. Serum concentration of 25-hydroxyvitamin D in autism spectrum disorder: a systematic review and meta-analysis. Eur Child Adolesc Psychiatry 2016;25(4):341–50.
[46] Kočovská E, et al. The rising prevalence of autism: a prospective longitudinal study in the Faroe Islands. J Autism Dev Disord 2012;42(9):1959–66.
[47] Fernell E, et al. Autism spectrum disorder and low vitamin D at birth: a sibling control study. Mol Autism 2015;6(1):3.
[48] Dealberto MJ. Prevalence of autism according to maternal immigrant status and ethnic origin. Acta Psychiatr Scand 2011;123(5):339–48.
[49] Chen J, Xin K, Wei J, Zhang K, Xiao H. Lower maternal serum 25 (OH) D in first trimester associated with higher autism risk in Chinese offspring. J Psychosom Res 2016;89:98–101.
[50] Schmidt RJ, et al. Selected vitamin D metabolic gene variants and risk for autism spectrum disorder in the CHARGE Study. Early Human Dev 2015;91(8):483–9.
[51] Coşkun S, Şimşek Ş, Camkurt MA, Çim A, Çelik SB. Association of polymorphisms in the vitamin D receptor gene and serum 25-hydroxyvitamin D levels in children with autism spectrum disorder. Gene 2016;588(2):109–14.
[52] Vinkhuyzen A, et al. Gestational vitamin D deficiency and autism-related traits: the Generation R Study. Mol Psychiatry 2016.
[53] Saad K, et al. Randomized controlled trial of vitamin D supplementation in children with autism spectrum disorder. J Child Psychol Psychiatry 2016.
[54] Jia F, Wang B, Shan L, Xu Z, Staal WG, Du L. Core symptoms of autism improved after vitamin D supplementation. Pediatrics 2015;135(1):e196–8.
[55] Stubbs G, Henley K, Green J. Autism: will vitamin D supplementation during pregnancy and early childhood reduce the recurrence rate of autism in newborn

siblings? Med Hypotheses 2016;88:74–8.
[56] Grant WB, Cannell JJ. Autism prevalence in the United States with respect to solar UV-B doses: an ecological study. Dermato-Endocrinology 2013;5(1):159–64.
[57] Grant WB, Soles CM. Epidemiologic evidence for supporting the role of maternal vitamin D deficiency as a risk factor for the development of infantile autism. Dermato-Endocrinology 2009;1(4):223–8.
[58] Mazahery H, Camargo CA, Conlon C, Beck KL, Kruger MC, von Hurst PR. Vitamin D and autism spectrum disorder: a literature review. Nutrients 2016;8(4):236.
[59] Kimlin MG. Geographic location and vitamin D synthesis. Mol Aspects Med 2008;29(6):453–61.
[60] K. Lawrence, M. Al-Jamal, I. Kohli, I. Hamzavi, Clinical and biological relevance of visible and infrared radiation. In: Principles and Practice of Photoprotection: Springer, 2016, pp. 3–22.
[61] D. Kulms, T. Schwarz, 20 years after-milestones in molecular photobiology. In: Journal of Investigative Dermatology Symposium Proceedings, 2002, vol. 7, no. 1, pp. 46–50: Elsevier.
[62] (2017). Data.GISS: Monthly Latitude Insolation. Available: http://data.giss.nasa.gov/ar5/srmonlat.html.
[63] Dekkers LM, Groot NA, Mosquera END, Zúniga IPA, Delfos MF. Prevalence of autism spectrum disorders in ecuador: a pilot study in quito. J Autism Dev Disord 2015;45(12):4165–73.
[64] Schelly D, González PJ, Solís PJ. The diffusion of autism spectrum disorder in Costa Rica: evidence of information spread or environmental effects? Health Place 2015;35:119–27.
[65] Poovathinal SA, et al. Prevalence of autism spectrum disorders in a semiurban community in south India. Ann Epidemiol 2016;26(9):663–5. e8.
[66] Fombonne E, et al. Prevalence of autism spectrum disorders in Guanajuato, Mexico: the leon survey. J Autism Dev Disord 2016;46(5):1669–85.
[67] Zahrani AA. Prevalence and clinical characteristics of autism spectrum disorders in school-age children in Taif-KSA. Int J Med Sci Public Health 2013;2(3):578–82.
[68] Paula CS, Ribeiro SH, Fombonne E, Mercadante MT. Brief report: prevalence of pervasive developmental disorder in Brazil: a pilot study. J Autism Dev Disord 2011;41(12):1738–42.
[69] Al-Farsi YM, Al-Sharbati MM, Al-Farsi OA, Al-Shafaee MS, Brooks DR, Waly MI. Brief report: Prevalence of autistic spectrum disorders in the Sultanate of Oman. J Autism Dev Disord 2011;41(6):821–5.
[70] Chien I-C, Lin C-H, Chou Y-J, Chou P. Prevalence and incidence of autism spectrum disorders among national health insurance enrollees in Taiwan from 1996 to 2005. J Child Neurol 2011;26(7):830–4.
[71] S.M. Fortea, B.M. Escandell, S.J. Castro, Estimated prevalence of autism spectrum disorders in the Canary Islands, In: Anales De Pediatria (Barcelona, Spain: 2003), 2013, vol. 79, no. 6, pp. 352–359.
[72] Raz R, Weisskopf MG, Davidovitch M, Pinto O, Levine H. Differences in autism spectrum disorders incidence by sub-populations in Israel 1992–2009: a total population study. J Autism Dev Disord 2015;45(4):1062–9.
[73] Raina SK, Kashyap V, Bhardwaj A, Kumar D, Chander V. Prevalence of autism spectrum disorders among children (1–10 years of age)-Findings of a mid-term report from Northwest India. J Postgrad Med 2015;61(4):243.
[74] Zeglam A, Maouna A. Prevalence of autistic spectrum disorders in Tripoli, Libya: the need for more research and planned services/Prévalence des troubles du spectre autistique à Tripoli (Libye): intensifier les travaux de recherche et les services planifiés. Eastern Mediterranean Health J 2012;18(2):184.
[75] Kamio Y, Haraguchi H, Stickley A, Ogino K, Ishitobi M, Takahashi H. Brief report: best discriminators for identifying children with autism spectrum disorder at an 18-month health check-up in Japan. J Autism Dev Disord 2015;45(12):4147–53.
[76] Chaaya M, Saab D, Maalouf FT, Boustany R-M. Prevalence of autism spectrum disorder in nurseries in Lebanon: a cross sectional study. J Autism Dev Disord 2016;46(2):514–22.
[77] T.A. Becerra et al., Autism spectrum disorders and race, ethnicity, and nativity: a population-based study, Pediatrics, pp. peds. 2013–3928, 2014.
[78] Kim YS, et al. Prevalence of autism spectrum disorders in a total population sample. Am J Psychiatry 2011;168(9):904–12.
[79] Sun X, et al. Exploring the underdiagnosis and prevalence of autism spectrum conditions in Beijing. Autism Res 2015;8(3):250–60.
[80] Bakian AV, Bilder DA, Coon H, McMahon WM. Spatial relative risk patterns of autism spectrum disorders in Utah. J Autism Dev Disord 2015;45(4):988–1000.
[81] van Bakel MME, et al. Low but increasing prevalence of autism spectrum disorders in a French area from register-based data. J Autism Dev Disord 2015;45(10):3255–61.
[82] L. Vehling, M. Brownell, J. Kaufert, N. Nickel, S. Alessi-Severini, Children with autism spectrum disorder in Manitoba: prevalence, population characteristics and psychotropic medication use, Health Promotion & Chronic Disease Prevention in Canada: Research, Policy & Practice, vol. 36, no. 11, 2016.
[83] Boilson A, Staines A, Ramirez A, Posada M, Sweeney M. Operationalisation of the European Protocol for Autism Prevalence (EPAP) for Autism Spectrum Disorder Prevalence Measurement in Ireland. J Autism Dev Disord 2016;46(9):3054–67.
[84] O'leary L, Henderson A, Jacobs M, Cooper S-A. Children with intellectual disabilities and children with autism in Scottish schools. J Intellectual Disability Res 2016;60(7–8):717.
[85] Idring S, et al. Changes in prevalence of autism spectrum disorders in 2001–2011: findings from the Stockholm youth cohort. J Autism Dev Disord 2015;45(6):1766–73.
[86] Saemundsen E, Magnússon P, Georgsdóttir I, Egilsson E, Rafnsson V. Prevalence of autism spectrum disorders in an Icelandic birth cohort. BMJ Open 2013;3(6):e002748.
[87] Wacker M, Holick MF. Sunlight and Vitamin D: a global perspective for health. Dermato-Endocrinology 2013;5(1):51–108.
[88] Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Am J Clin Nutr 2004;79(3):362–71.
[89] O'Neill CM, et al. Seasonal changes in vitamin D-effective UVB availability in Europe and associations with population serum 25-hydroxyvitamin D. Nutrients 2016;8(9):533.
[90] Stalgis-Bilinski KL, Boyages J, Salisbury EL, Dunstan CR, Henderson SI, Talbot PL. Burning daylight: balancing vitamin D requirements with sensible sun exposure. Med J Aust 2011;194(7):345.
[91] Seckmeyer G, et al. A novel method to calculate solar UV exposure relevant to vitamin D production in humans. Photochem Photobiol 2013;89(4):974–83.
[92] Rosero-Bixby L. Spatial access to health care in Costa Rica and its equity: a GIS-based study. Soc Sci Med 2004;58(7):1271–84.
[93] W.D. Savedoff, A moving target: universal access to healthcare services in Latin America and the Caribbean, Working paper//Inter-American Development Bank, Research Department 2009.
[94] Parisi AV, Turnbull DJ, Turner J. Influence of clouds on pre-vitamin D3 effective solar UV exposures. Environ Health 2007;7(3):75.
[95] F. Alagol. Y. Shihadeh, H. Boztepe, R. Tanakol, S. Yarman, H. Azizlerli, O. Sandalci, Sunlight exposure and vitamin D deficiency in Turkish women, J Endocrinol Invest, 23(3):173–7.
[96] Summary Statistics for Schools in Scotland, No. 7: 2016 Edition, National Statistics2016, Available: http://www.gov.scot/Publications/2016/12/9271/downloads#res511474.
[97] (2017). Web Resource on Autism Spectrum Disorders (ASDs) For General Practitioners and Primary Care Practitioners. Available: http://asd.nes.scot.nhs.uk/1144.
[98] C.-R. Jung, Y.-T. Lin, B.-F. Hwang, Air pollution and newly diagnostic Autism Spectrum Disorders: a population-based cohort study in Taiwan. Plos One, Sept., 2013. doi: 10.1371/journal.pone.0075510.
[99] Shane HC, Albert PD. Electronic screen media for persons with autism Spectrum Disorders: results of a survey. J Autism Dev Disord 2008;38:1499–508.
[100] W. Chonchaiya, P. Nuntnarumit, C. Pruksananonda, Comparison of television viewing between children with autism spectrum disorder and controls, Acta Paediatrica, 100, 1033–7.
[101] Bent CA, Dissanayake C, Barbaro J. Mapping the diagnosis of autism spectrum disorders in children aged under 7 years in Australia, 2010–2012. Med J Australia 2015;202(6):317–20.