Published in final edited form as:
Neurotoxicology. 2009 September ; 30(5): 822–831. doi:10.1016/j.neuro.2009.01.011.

Associations between indoor environmental factors and parental-reported autistic spectrum disorders in children 6-8 years of age

Malin Larsson[a], **Bernard Weiss**[b], **Staffan Janson**[a], **Jan Sundell**[c,d], and **Carl-Gustav Bornehag**[a,c,f]

[a]Karlstad University, Health and Environmental Sciences, Sweden

[b]Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester NY USA

[c]Technical University of Denmark, International Centre for Indoor Environment and Energy, Denmark

[d]University of Texas at Tyler, USA

[e]County Council of Värmland, Sweden

[f]SP Technical Research Institute of Sweden

Abstract

Potential contributions of environmental chemicals and conditions to the etiology of Autism Spectrum Disorders are the subject of considerable current research and speculation. The present paper describes the results of a study undertaken as part of a larger project devoted to the connection between properties of the indoor environment and asthma and allergy in young Swedish children. The larger project, *The Dampness in Buildings and Health (DBH) Study*, began in the year 2000 with a questionnaire distributed to parents of all children 1-6 years of age in one Swedish county (DBH-I). A second, follow-up questionnaire (DBH-III) was distributed in 2005. The original survey collected information about the child, the family situation, practices such as smoking, allergic symptoms, type of residence, moisture-related problems, and type of flooring material, which included polyvinyl chloride (PVC). The 2005 survey, based on the same children, now 6-8 years of age, also asked if, during the intervening period, the child had been diagnosed with Autism, Asperger's syndrome, or Tourette's syndrome. From a total of 4,779 eligible children, 72 (60 boys, 12 girls) were identified with parentally-reported autism spectrum disorder. A random sample of 10 such families confirmed that the diagnoses had been made by medical professionals, in accordance with the Swedish system for monitoring children's health. An analysis of the associations between indoor environmental variables in 2000 as well as other background factors and the ASD diagnosis indicated five statistically significant variables: (1) maternal smoking; (2) male sex; (3) economical problems in the family; (4) condensation on windows, a proxy for low ventilation rate in the home; (5) PVC flooring, especially in the parents' bedroom. In addition, airway symptoms of wheezing and physician-diagnosed asthma in the baseline investigation (2000) were associated with ASD five years later. Results from the second phase of

Corresponding author: Bernard Weiss, Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester NY 14642, bernard_weiss@urmc.rochester.edu, tel: 585-275-1736; fax: 585-256-2591.

Conflict of Interest Statement: The study was funded by grants from the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (Formas), Swedish Asthma and Allergy Association's Research Foundation, and the Swedish Foundation for Health Care Sciences and Allergy Research. The participation of B. Weiss was supported in part by NIEHS grants ES013247 and ES015509 and Center grant ES01247.

the DBH-study (DBH-II) indicate PVC flooring to be one important source of airborne phthalates indoor, and that asthma and allergy prevalence are associated with phthalate concentrations in settled dust in the children's bedroom. Because these associations are among the few linking ASD with environmental variables, they warrant further and more extensive exploration.

Keywords

Allergy; Asthma; Autism spectrum disorders; Phthalates; Polyvinyl chloride (PVC)

Introduction

Over the past few decades, our understanding of the genesis and character of autism has undergone a series of transformations. It is now viewed, not as a unitary disorder, but as one with multiple dimensions (hence the term, *autism spectrum disorder, ASD*), displaying many degrees of severity, and attributable to a variety of potential causes. We now recognize that its manifestations touch many organ systems as well as the brain. We still view it as rooted in genetics, but subject as well to environmental events and circumstances. Exposures to aberrant environmental conditions and to chemical contaminants, in particular, are now seen as possible factors in its etiology.

The current report emphasizes one class of conditions and contaminants; in essence, those arising from the indoor environment, which could be relevant from an exposure point of view since we spend most of our time in such environments. The report is one of a series directed originally at how certain properties of the indoor environment, such as moisture related problems and different building materials are associated with allergies and asthma in Swedish children. Almost adventitiously, the investigation uncovered an apparent association between certain of these properties and medically diagnosed ASD. The data are far from conclusive. They are puzzling, even baffling, and not readily explicable at this time. However, because they are among the few clues that have emerged about possible environmental contributions to autistic disorders, we believe that they should be weighed carefully and warrant further study.

Background

The global incidence of allergy and asthma has risen substantially over the past three decades (Beasley, 2002; Beggs and Bambrick, 2005), as it has in Swedish children. One possible factor contributing to this rise, noted repeatedly in the literature, is the character of the indoor environment and exposures occurring in that setting. Because moisture-related problems or “dampness” have been associated with respiratory symptoms and with allergy and asthma in numerous studies (reviewed in Bornehag et al., 2005b) a consortium of Swedish organizations and institutions undertook an epidemiological study designated the “Dampness in Buildings and Health” study (DBH). DBH began in 2000. Its central aim is to determine elements of the indoor environment associated with asthma and allergic symptoms among small children and their parents. The choice of young children as the study population arose from two considerations. First, preschool children display a higher incidence of allergies than adults. Second, most of their time is spent in the home, the environment that is the focus of the effort. The data reported here represent one set of DBH findings. They describe associations between ASD in children aged 6-8 years and a number of environmental factors, including exposure conditions when they were 1-3 years of age and, almost surely, during pregnancy and the first year of life.

Method

The Dampness in Buildings and Health (DBH) study has so far embodied three phases.

- DBH-I, a cross-sectional study based on a questionnaire sent to parents of 14,077 children in the county of Värmland in 2000 (Bornehag et al., 2004a).
- DBH-II, a nested case-control study of 198 symptomatic children and 202 healthy controls from DBH-I (Bornehag et al., 2004b).
- DBH-III, a 5-year follow-up study of those eligible for DBH-I, conducted in 2005.

The data in the current paper are based on the initial baseline study (DBH-I) and the 5-year follow-up (DBH-III) (Larsson et al., 2008).

Study population

In DBH-I, a questionnaire was distributed to the parents of all children 1-6 years of age (n=14,077) in the county of Värmland, Sweden, in March 2000. 10,851 answers were collected, corresponding to a response rate of 79% representing 8,918 families. An analysis of non-responders revealed no indications of selection bias (Bornehag et al., 2006). Five years after the first questionnaire, in March 2005, a follow-up questionnaire was distributed in accordance with phase III of DBH. It was sent to the first three-year groups eligible to participate in DBH-I, i.e., those children 1, 2 and 3 years of age in 2000 and 6, 7, and 8 years of age in 2005 (n=7,509). A total of 5,483 responses, corresponding to a response rate of 73%, were received. Of these, 4,779 children participated in both the baseline (DBH-I) and the follow-up study (DBH-III) and therefore constitute the study population for the current paper.

Questionnaire

The baseline survey consisted of 84 questions about the child (e.g., age, sex, birth weight, length of breast-feeding), the family situation, such as number of family members, and such practices as smoking in the home. Information about allergic symptoms among children was collected with the same questions used in the ISAAC (International Study of Asthma and Allergies in Childhood) studies (Pearce et al., 2007). Items about the home and its surroundings, e.g., type and area of the residence, moisture-related problems (condensation on the inside of the window pane during heating season), and type of flooring material (PVC, wood, linoleum, other) were included. Such data were mainly collected in the baseline questionnaire.

The 2005 follow-up study also included the results of a standard pediatric questionnaire. One section of that questionnaire contained an item about a variety of disorders:

Has your child had any of the following diseases/disorders during the last 12 months?

a. visual impairment - no/yes

b. hearing impairment

c. speech defect

d. diabetes

e. mental illness

f. epilepsy

g. stomach pain

h. asthma

i. allergic rhinitis

j. eczema

k. physical dysfunction

l. overweight

m. ADHD

n. Autism, Asperger or Tourette's syndrome

o. other disorders or problems

Question (n) treats these three disorders under one heading because research in Sweden indicates a high degree of comorbidity. That is, according to Kadesjö and Gillberg (Kadesjo and Gillberg, 2000), “Attention deficits and empathy/autism spectrum problems (including Asperger's disorder) [are] very common, each type of comorbidity affecting approximately two thirds of individuals with Tourette's disorder.”

Question (n) elicited 72 positive responses. Of these, 60 were boys and 12 were girls. Among those who provided positive responses, a telephone interview was conducted with 10 randomly selected families (8 boys and 2 girls). All had received a clinical diagnosis of such a disorder (eight with autism, one with Asperger, and one with Tourette's syndrome) before the 2005 questionnaire was distributed, as well as a confirmation of that diagnosis after the questionnaire responses had been submitted.

Statistical analyses

Associations between family structure, specified family behaviors, environmental and socioeconomic factors and ASD were estimated by using univariate tests (χ^2) and multiple logistic regressions. Results are expressed as crude odds ratios (OR) and adjusted odds ratios (*a*OR) with 95% confidence intervals. In the multivariate analyses, adjustments were made for sex, age of the child (6, 7, or 8 years old), any smoking in mother (smoking during pregnancy and/or smoking during the child's first year and/or current smoking vs. no smoking in the mother), asthma in the child 2000 (no vs. yes), financial insecurity expressed as problems with paying bills (no, yes, no reply), and condensation on the inside of the windows in the child's room during winter time as a proxy for low ventilation (no, 1-5 cm, >5 cm). Most of the analyses examined associations based on responses from the baseline questionnaire in 2000 and ASD five years later, as reflected in the follow-up study. Other analyses were necessarily based on data available only from the follow-up questionnaire. All analyses were considered to be statistically significant when the p-value was less than 0.05. Statistical analyses were carried out using SPSS for Windows (version 14.0).

The study was approved by the ethical committee in Örebro, Sweden.

Results

Of the 4,779 children in the study, 50% were girls (n=2,391) and age was evenly distributed among the participants (Table 1). A variety of changes occurred in family conditions and circumstances between 2000 and 2005. In 2000, 81% of the families lived in a single-family house; five years later this figure had increased to 86%. The proportion of homes larger than 150 square meters increased from about 21% to 28%. The most common type of flooring in the child's and the parent's bedroom in 2000 was PVC flooring, while in 2005 wood flooring was most commonly reported. Reports of more than 5 cm condensation on the inside surface of windows during the heating season (an indication of low ventilation rate in the room) in

the child's, the parent's and the living room decreased during these five years. In 2000, almost 7% of the children lived with only one parent, while 5 years later this figure had risen to about 20%. Smoking among the parents decreased in this population from 14.1% to 12.7% for mothers and from 10.4% to 8.3% for fathers during the five-year period. Data on the socioeconomic status of the family were collected only in the follow-up study. More than 10% of the families reported problems with paying bills during the last 12 months. Almost 4% of the total population answered that the disease of the child had reduced their financial status. More than half the study population (53.6%) reported symptoms of allergy (asthma, rhinitis and/or eczema) in the family (mother and/or father and/or siblings).

The 72 children with parentally-reported ASD correspond to a prevalence of 1.5%. As noted earlier, ASD was five times more common among boys. It was slightly more common among older children. Children with ASD had fewer siblings than those without (Table 2).

Different proxies for lower socioeconomic status in the family, namely, divorce and financial problems, were significantly associated with ASD (Table 3). Past or current smoking by mothers, but not fathers, was significantly associated with ASD.

Airway symptoms of wheezing and physician-diagnosed asthma in the baseline investigation (2000) were significantly associated with ASD five years later in crude analyses and marginally in the adjusted analyses (Table 4). The analysis of symptoms reported in 2005 uncovered statistically significant associations between ASD and physician-diagnosed asthma in both crude and adjusted analyses.

A significant association between maternal eczema in 2000 and ASD in the child in 2005 appeared (Table 5), but no such association with paternal symptoms emerged. Reports of sick building syndrome (SBS) symptoms among parents in 2000 were associated with children's ASD five years later, with statistically significant results for concentration difficulties, irritation in eyes and skin problems in face and head (Table 6).

Certain indoor environmental factors from the child's home were associated with ASD in crude analyses (Table 7). A greater proportion of children with ASD were reported to have PVC as flooring material in the child's and the parent's bedroom in 2000 compared to children without ASD. Furthermore, children with ASD were reported to live in homes with more condensation on the inside of the windows, which, as noted earlier, may be seen as an indicator for deficient ventilation.

Finally, when data were analysed in a multivariate model, several of the reported associations from the crude analyses remained (Table 8). Two different models were used for child's bedroom and for parents' bedroom: 1. PVC vs. all flooring types adjusted for all other factors listed; 2. PVC vs. wood adjusted for all other factors listed.

ASD was significantly associated with male sex, financial problems in the family (2005), maternal smoking, and PVC as flooring material (in the parent's bedroom) as well as condensation on the inside of the windows during the winter time. Adjusted associations between ASD and type of flooring material became stronger when PVC as flooring material was compared with wood compared to when PVC was compared with all other flooring materials (i.e., wood, linoleum, stone or wall-to-wall carpet).

Discussion

At this time, we lack any firm knowledge about the extent to which environmental chemicals or other environmental conditions might influence the etiology or manifestations of ASDs. That is, using the terminology of cancer risk assessment, do they act primarily as

initiators, or primary causes, or are they more like promotors, simply enhancing or amplifying a process already underway or is it just a matter of confounding? For other neurodevelopmental endpoints, the past few decades have demonstrated convincingly that "normal" development is vulnerable to a variety of environmental chemicals. They include metals, pesticides, plasticizers, solvents (and alcohol), organohalogen compounds, and many other chemicals to which virtually all humans in developed countries are exposed. The length of the list of industrial chemicals and their metabolites found in the U.S. population, and published in the NHANES data base is staggering (CDC).

The current study found 72 children with parentally-reported ASD, corresponding to a prevalence of 1.5%. Such a figure is slightly higher than that reported in several other studies that showed ASD prevalence rates in the range of 0.3 to 1.2% (Baird et al., 2006; Bertrand et al., 2001; Fombonne, 2005; Gillberg et al., 2006; Rutter, 2005). However, in a recent study on 9,430 children (7-9 y) in Bergen, Norway, parents completed an autism spectrum screening questionnaire (ASSQ), which consists of 27 items scored on a 3-point scale. The authors found an ASD prevalence of 1.8% based on this instrument. Tourette's syndrome was not included in the ASD definition used in that study (Posserud et al., 2006). It is conceivable, too, that ASD may be underreported since non-responding families exhibit a significantly higher prevalence of autism than responding families (Posserud et al., 2006).

What is novel about our data are the statistically significant links between the diagnosis of ASD and certain factors in the child's early environment. The most unexpected of these factors is flooring type. PVC flooring is an important source of airborne phthalates, already documented to be associated with asthma and allergy responses (Bornehag et al., 2004a; Bornehag et al., 2004b; Jaakkola and Knight, 2008). The greater the number of rooms covered by PVC flooring, the higher the levels of phthalates in dust.

Condensation on the inside of windows was also associated with ASD. Condensation, we believe, serves as an index of low air exchange rate in the home more than it serves as an independent risk factor. A low rate of exchange in the home will, in essence, increase indoor exposures to tobacco smoke and many other chemical (and biological) pollutants, including phthalates.

In interpreting these results, it is important to recognize that the diagnosis of neurodevelopmental disorders in Sweden is highly structured, unlike the system prevailing in the U.S. Virtually every pregnancy and every child are assessed with periodic examinations. The Swedish system embodies the following steps:

- >99.5% of all pregnant women are followed during pregnancy
- 95% start their controls in gestational week 10
- >99.5% of all children are followed at county level well baby clinics
- Nurses and GPs are given special pediatric training
- In every county, a pediatrician supervises the well baby clinics
- Physicians and nurses are trained to assess psychomotor development
- Assessment of autism was introduced in the 1980s
- Suspected cases are referred to a special neuropsychiatric team
- Practically all children with NP disorders are diagnosed before beginning school

Although we are confident about the clinical accuracy of the ASD diagnosis, our questionnaire data provide no information on when the disorder was detected or diagnosed.

Abnormalities in social and cognitive function may have been present early in development or might have emerged much later. Within these limitations, the term, “incidence,” could be deceptive. For example, parental awareness of abnormal behavior may increase as the child ages, as indicated in Table 2, which shows a higher prevalence for older children. Until recently, however, a diagnosis of autism was relatively infrequent in children less than three years of age. Quite often, the diagnosis was not established until primary school or kindergarten, where the more demanding and less familiar environment would highlight the child's social and cognitive deficiencies (Landa, 2008). Based on these considerations, we believe that our questionnaire data on environmental factors and lifestyles at baseline, collected for DBH-I, reflect the family's status prior to the formal diagnosis of ASD and provide a window on prenatal factors. Such a displacement in time should reduce the risk for recall bias. All the same, we recognize that the parents may have been aware of the child's problems at baseline, despite the lack of a formal diagnosis, and may have responded to the questionnaire in a systematically different way from parents whose children displayed no overt problems. In such a case, the risk for recall bias remains. Even so, we believe that associations between factors prevailing at baseline (2000) and parental reports of ASD five years later are more compelling and valid than those based on associations from cross-sectional data in the follow-up study. The exceptions consist of the effects that an ASD child may exert on factors such as economic stress and family unity. The follow-up data present a greater chance of confounding environmental and lifestyle factors with ASD because they were collected at the same time.

Another reason for our confidence in these results is the association we found with smoking. Smoking, especially during pregnancy, is a well-documented risk factor for child behaviour problems, including ASD (Fergusson et al., 1998; Indredavik et al., 2007; Linnet et al., 2003; Wakschlag et al., 2002; Williams et al., 1998). A case-control study showed daily maternal smoking during early pregnancy to be linked to autism in the child (Hultman et al., 2002). Our study confirms that prenatal smoking and smoking during the child's first year of life can be coupled to ASD. Further, since data on smoking during this early life period were collected at baseline, we strongly suspect that tobacco smoke exposure occurred before the diagnosis of ASD, limiting the probability of recall bias. Similarly, the data collected in 2000, when the children were 1-3 years of age, almost certainly reflect conditions prevailing during pregnancy.

Children with ASD were reported to have around twice the odds of airway symptoms (i.e., wheezing and doctor diagnosed asthma) compared to children without ASD. Such an association could be seen in both the baseline and the follow up data. The mechanism for this association is not obvious. It is interesting to point out that boys have more doctor-diagnosed asthma than girls in the age range 6-8 years (11.8 vs. 5.6%, $p<0.001$ in the current study), and a similar pattern is evident for ASD (Fombonne, 1999; Wong and Hui, 2008; Yeargin-Allsopp et al., 2003); i.e., boys suffer more from both asthma/allergy and ASD. However, in the current data, the association between asthma and ASD was mainly found for girls. Of the 12 girls with ASD, 27.3% (3 girls) were reported to have doctor-diagnosed asthma at baseline compared to 3.6% asthma among girls without ASD. Among the 60 boys with ASD, 5 had asthma at baseline, corresponding to a prevalence of 8.3% compared to 6.8% among boys without ASD.

The reason why allergic symptoms in the mothers at baseline were weakly associated with ASD in the child while such problems among the fathers were not associated at all is not obvious. However, such associations have been reported in a study from the U.S., where the risk for ASD doubled in the offspring of mothers with allergic diseases during pregnancy (Croen et al., 2005), indicating that such diseases could be associated with ASD. A number of potential mechanisms for such an association can be extracted from the

neurodevelopmental literature, for example, those studies showing associations between schizophrenia risk and maternal infections (Brown and Susser, 2002; Meyer et al., 2005). Infections, of course, activate the immune system, whose potential links to ASDs have been the subject of many recent publications (Becker, 2007; Fatemi et al., 2008; Gregg et al., 2008; Pessah et al., 2008).

Our study showed that families with an ASD child report more economic problems and proxies for lower economic status, such as living in multi-family house and a smaller size home, compared with families without an ASD child. Unfortunately, data on economic problems (i.e., problems in paying bills) were only collected in the follow-up study, meaning that we cannot establish temporal relationships. Information about the type of building and size of the home were collected both at baseline and at follow up. Here there are indications of a stronger association between ASD and these factors in data from 2005 compared to data from 2000, indicating that economic problems are more likely a result of ASD rather than a risk factor. Divorce in the family (i.e., most often a single motherhood), which in Sweden is associated with lower socioeconomic status (Fritzell et al., 2007), was also a stronger risk factor in the 2005 data, compared to the 2000 data, indicating again that divorce and associated financial problems are more a result of ASD disorder in the family than the opposite. It is well known that parents with children that are disabled or have chronic diseases are more apt to divorce. However, one complicating issue is that smoking is more common in families with lower socioeconomic status. For example, in the families experiencing divorce, about 23% of the mothers smoked while only 10% smoked in families where the child lived with both parents. In families that often have problems in paying bills, 37% of the mothers smoked while 25% of the mothers smoked in families that sometimes have problem with paying bills and in families without such problems only about 11% smoked. Therefore, it is difficult to separate the effects of socioeconomic status from those of smoking when considering risk for ASD.

Sick Building Syndrome is applied to a situation in which occupants of a building complain of nonspecific symptoms such as headache, dizziness, nausea, difficulty concentrating, eye or throat irritation, cough, and dry or itchy skin. It is assumed to result from factors such as inadequate ventilation, chemical contaminants, and biological contaminants. We used the list in Table 6 as an index of comfort level, so to speak, in the home environment which might then be traced more specifically to the indoor environmental variables.

The prevalence of parents' reports of sick building syndrome symptoms (SBS) is in accordance with other studies (Eriksson and Stenberg, 2006). There was a tendency for parents of ASD children to report more SBS symptoms than other parents. It is important to point out that the SBS reports come from the baseline investigation (2000), meaning that reports of SBS symptoms most probably are not a result of a subsequent ASD diagnosis in the child.

Perhaps the most intriguing of our findings is that PVC flooring material in the home, when the child was 1-3 years of age, was associated with ASD five years later. In accordance with the discussion above, even if a parent knew that their child had ASD at baseline, there is no reason to believe that parent's reports on type of flooring would be biased in the absence of any discussion of the relationship between type of flooring or building material and ASD. PVC flooring, however, might be seen as a proxy for lower socioeconomic status in Swedish society. As said earlier, socioeconomic factors may be a result of ASD in the family while PVC flooring was associated with ASD more strongly at baseline than in the follow-up study five years later. Another finding indicated that PVC flooring in the parent's bedroom showed a stronger association with ASD compared to PVC flooring in the child's bedroom. Many children in Sweden sleep in their parent's bedroom during the first years of life, so

that one explanation for the association could be that children with problems in their cognitive functioning more often sleep with their parents and for a longer period of time compared with children without ASD. We also found that ASD children slightly more often slept in the parent's bedroom compared with other children at baseline (47.9 vs. 43.2%).

As reported by Bornehag (Bornehag et al., 2005c) it is uncommon to find wall-to-wall carpeting in Swedish homes. They estimated a frequency of less than half a percent. In contrast, floors in U.S. homes, especially newer models, most often are carpeted, except for kitchens and bathrooms, because wood flooring is considerably more expensive. Hwang (Hwang et al., 2008) found indoor dust samples highly contaminated by phthalates such as di-(2-ethylhexyl) phthalate (DEHP). Mendell (Mendell, 2007) summarized 21 epidemiologic studies on associations between indoor residential chemical emissions, or emission-related materials or activities, and respiratory health or allergy in infants or children. Strong associations were reported between many risk factors and respiratory or allergic effects. Risk factors identified most frequently included formaldehyde or particleboard, phthalates or plastic materials, and recent painting. Other studies have also found tributyl tin, pyrethroids, and Polybrominated Diphenyl Ethers (PBDEs) in carpets. The U.S. situation, for this reason, may magnify the associations with ASD reported here, and, we believe, deserves at least exploratory investigations.

Phase II of the DBH study showed that PVC flooring is one important source of phthalates in indoor dust in Swedish homes (Bornehag et al., 2005a). Moreover, exposure to selected phthalate esters in indoor dust was associated with asthma in children in a dose-response relationship (Bornehag et al., 2004b), a result confirmed in a DBH-study in Bulgaria (Kolarik et al., 2008). These findings evoke the question of potential mechanisms. Phthalates are viewed as potential endocrine-disrupting chemicals, acting as anti-androgens to disrupt male development (Wilson et al., 2008). At the same time, it has been suggested that phthalates can induce asthma and allergic responses (Jaakkola and Knight, 2008). The challenge to investigators is to define how these toxic manifestations might be connected to the etiology or expression of ASDs.

Up to now, no environmental factors have been documented in the etiology of ASDs. Although gestational exposures to thalidomide (Stromland and Miller, 1993) and valproic acid (Christianson et al., 1994) are risk factors for ASDs, they can hardly be considered environmental sources. Their main value, similar to the role that MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) played in Parkinson's disease (Langston, 1985, Langston et al., 1999) is to illustrate the possibility that exogenous chemicals may be risk factors for the disease.

A limitation of this study is that we have only parental reports of ASD from a questionnaire with limited confirmatory information. However, our validation study of ten families showed that the parental reports of ASD in the questionnaire reflected a clinical diagnosis of ASD by medical professionals. Furthermore, our experience tells us that there is no reason to believe that the parents would report autism, Asperger or Tourette's syndrome without a clinical diagnosis or other relevant information as a basis for their reports. We also believe that our data on ASD are valid because our estimated prevalence is in accordance with other studies, and associated factors, such as male sex and smoking among mothers, are in agreement with findings from other studies. The association of PVC flooring with ASD, which we presume to reflect exposure to airborne phthalates, suggests that studies of other chemical contaminants with endocrine disruptor properties might yield useful insights into the genesis of ASDs.

Acknowledgments

The study was funded by grants from the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (Formas), Swedish Asthma and Allergy Association's Research Foundation, and the Swedish Foundation for Health Care Sciences and Allergy Research. The participation of B. Weiss was supported in part by NIEHS grants ES013247 and ES015509 and Center grant ES01247.

References

Baird G, Simonoff E, Pickles A, Chandler S, Loucas T, Meldrum D, Charman T. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). Lancet. 2006; 368:210–215. [PubMed: 16844490]

Beasley R. The burden of asthma with specific reference to the United States. J Allergy Clin Immunol. 2002; 109:S482–489. [PubMed: 11994720]

Becker KG. Autism, asthma, inflammation, and the hygiene hypothesis. Med Hypotheses. 2007; 69:731–740. [PubMed: 17412520]

Beggs PJ, Bambrick HJ. Is the global rise of asthma an early impact of anthropogenic climate change? Environ Health Perspect. 2005; 113:915–919. [PubMed: 16079058]

Bertrand J, Mars A, Boyle C, Bove F, Yeargin-Allsopp M, Decoufle P. Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. Pediatrics. 2001; 108:1155–1161. [PubMed: 11694696]

Bornehag CG, Lundgren B, Weschler CJ, Sigsgaard T, Hägerhed-Engman L, Sundell J. Phthalates in indoor dust and their association with building characteristics. Environ Health Perspect. 2005a; 113:1399–1404. [PubMed: 16203254]

Bornehag CG, Sundell J, Hägerhed-Engman L, Sigsggard T, Janson S, Aberg N. 'Dampness' at home and its association with airway, nose, and skin symptoms among 10,851 preschool children in Sweden: a cross-sectional study. Indoor Air. 2005b; 15(Suppl 10):48–55. [PubMed: 15926944]

Bornehag CG, Sundell J, Sigsgaard T. Dampness in buildings and health (DBH): Report from an ongoing epidemiological investigation on the association between indoor environmental factors and health effects among children in Sweden. Indoor Air. 2004a; 14(Suppl 7):59–66. [PubMed: 15330773]

Bornehag CG, Sundell J, Sigsgaard T, Janson S. Potential self-selection bias in a nested case-control study on indoor environmental factors and their association with asthma and allergic symptoms among pre-school children. Scand J Public Health. 2006; 34:534–543. [PubMed: 16990165]

Bornehag CG, Sundell J, Weschler CJ, Sigsgaard T. Potential selection biases. Environ Health Perspect. 2005c; 113:A152–153. [PubMed: 15743700]

Bornehag CG, Sundell J, Weschler CJ, Sigsgaard T, Lundgren B, Hasselgren M, Hägerhed-Engman L. The association between asthma and allergic symptoms in children and phthalates in house dust: a nested case-control study. Environ Health Perspect. 2004b; 112:1393–1397. [PubMed: 15471731]

Brown AS, Susser ES. In utero infection and adult schizophrenia. Ment Retard Dev Disabil Res Rev. 2002; 8:51–57. [PubMed: 11921387]

CDC. Chemicals measured in selected participants for NHANES 2003-2004. Retrieved 2008-10-22, from http://www.cdc.gov/ExposureReport/pdf/NHANES03-04List_03_2007.pdf

Christianson AL, Chesler N, Kromberg JG. Fetal valproate syndrome: clinical and neurodevelopmental features in two sibling pairs. Dev Med Child Neurol. 1994; 36:361–369. [PubMed: 7512516]

Croen LA, Grether JK, Yoshida CK, Odouli R, Van de Water J. Maternal autoimmune diseases, asthma and allergies, and childhood autism spectrum disorders: a case-control study. Arch Pediatr Adolesc Med. 2005; 159:151–157. [PubMed: 15699309]

Eriksson NM, Stenberg BG. Baseline prevalence of symptoms related to indoor environment. Scand J Public Health. 2006; 34:387–396. [PubMed: 16861189]

Fatemi SH, Reutiman TJ, Folsom TD, Huang H, Oishi K, Mori S, Smee DF, Pearce DA, Winter C, Sohr R, Juckel G. Maternal infection leads to abnormal gene regulation and brain atrophy in mouse offspring: implications for genesis of neurodevelopmental disorders. Schizophr Res. 2008; 99:56–70. [PubMed: 18248790]

Fergusson DM, Woodward LJ, Horwood LJ. Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. Arch Gen Psychiatry. 1998; 55:721–727. [PubMed: 9707383]

Fombonne E. The epidemiology of autism: a review. Psychol Med. 1999; 29:769–786. [PubMed: 10473304]

Fombonne E. Epidemiology of autistic disorder and other pervasive developmental disorders. J Clin Psychiatry. 2005; 66(Suppl 10):3–8. [PubMed: 16401144]

Fritzell S, Ringback Weitoft G, Fritzell J, Burstrom B. From macro to micro: the health of Swedish lone mothers during changing economic and social circumstances. Soc Sci Med. 2007; 65:2474–2488. [PubMed: 17764795]

Gillberg C, Cederlund M, Lamberg K, Zeijlon L. Brief report: "the autism epidemic". The registered prevalence of autism in a Swedish urban area. J Autism Dev Disord. 2006; 36:429–435. [PubMed: 16568356]

Gregg JP, Lit L, Baron CA, Hertz-Picciotto I, Walker W, Davis RA, Croen LA, Ozonoff S, Hansen R, Pessah IN, Sharp FR. Gene expression changes in children with autism. Genomics. 2008; 91:22–29. [PubMed: 18006270]

Hultman CM, Sparen P, Cnattingius S. Perinatal risk factors for infantile autism. Epidemiology. 2002; 13:417–423. [PubMed: 12094096]

Hwang HM, Park EK, Young TM, Hammock BD. Occurrence of endocrine-disrupting chemicals in indoor dust. Sci Total Environ. 2008; 404:26–35. [PubMed: 18632138]

Indredavik MS, Brubakk AM, Romundstad P, Vik T. Prenatal smoking exposure and psychiatric symptoms in adolescence. Acta Paediatr. 2007; 96:377–382. [PubMed: 17407460]

Jaakkola JJ, Knight TL. The role of exposure to phthalates from polyvinyl chloride products in the development of asthma and allergies: a systematic review and meta-analysis. Environ Health Perspect. 2008; 116:845–853. [PubMed: 18629304]

Kadesjo B, Gillberg C. Tourette's disorder: epidemiology and comorbidity in primary school children. J Am Acad Child Adolesc Psychiatry. 2000; 39:548–555. [PubMed: 10802971]

Kolarik B, Naydenov K, Larsson M, Bornehag CG, Sundell J. The association between phthalates in dust and allergic diseases among Bulgarian children. Environ Health Perspect. 2008; 116:98–103. [PubMed: 18197306]

Landa RJ. Diagnosis of autism spectrum disorders in the first 3 years of life. Nat Clin Pract Neurol. 2008; 4:138–147. [PubMed: 18253102]

Langston JW. MPTP neurotoxicity: an overview and characterization of phases of toxicity. Life Sci. 1985; 36:201–206. [PubMed: 2857048]

Langston JW, Forno LS, Tetrud J, Reeves AG, Kaplan JA, Karluk D. Evidence of active nerve cell degeneration in the substantia nigra of humans years after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine exposure. Ann Neurol. 1999; 46:598–605. [PubMed: 10514096]

Larsson M, Hagerhed-Engman L, Sigsgaard T, Janson S, Sundell J, Bornehag CG. Incidence rates of asthma, rhinitis and eczema symptoms and influential factors in young children in Sweden. Acta Paediatr. 2008; 97:1210–1215. [PubMed: 18624993]

Linnet KM, Dalsgaard S, Obel C, Wisborg K, Henriksen TB, Rodriguez A, Kotimaa A, Moilanen I, Thomsen PH, Olsen J, Jarvelin MR. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. Am J Psychiatry. 2003; 160:1028–1040. [PubMed: 12777257]

Mendell MJ. Indoor residential chemical emissions as risk factors for respiratory and allergic effects in children: a review. Indoor Air. 2007; 17:259–277. [PubMed: 17661923]

Meyer U, Feldon J, Schedlowski M, Yee BK. Towards an immuno-precipitated neurodevelopmental animal model of schizophrenia. Neurosci Biobehav Rev. 2005; 29:913–947. [PubMed: 15964075]

Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, Robertson C. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2007; 62:758–766. [PubMed: 17504817]

Pessah IN, Seegal RF, Lein PJ, LaSalle J, Yee BK, Van De Water J, Berman RF. Immunologic and neurodevelopmental susceptibilities of autism. Neurotoxicology. 2008; 29:532–545. [PubMed: 18394707]

Posserud MB, Lundervold AJ, Gillberg C. Autistic features in a total population of 7-9-year-old children assessed by the ASSQ (Autism Spectrum Screening Questionnaire). J Child Psychol Psychiatry. 2006; 47:167–175. [PubMed: 16423148]

Rutter M. Incidence of autism spectrum disorders: changes over time and their meaning. Acta Paediatr. 2005; 94:2–15. [PubMed: 15858952]

Stromland K, Miller MT. Thalidomide embryopathy: revisited 27 years later. Acta Ophthalmol (Copenh). 1993; 71:238–245. [PubMed: 8333272]

Wakschlag LS, Pickett KE, Cook E Jr, Benowitz NL, Leventhal BL. Maternal smoking during pregnancy and severe antisocial behavior in offspring: a review. Am J Public Health. 2002; 92:966–974. [PubMed: 12036791]

Williams GM, O'Callaghan M, Najman JM, Bor W, Andersen MJ, Richards D, U C. Maternal cigarette smoking and child psychiatric morbidity: a longitudinal study. Pediatrics. 1998; 102:e11. [PubMed: 9651463]

Wilson VS, Blystone CR, Hotchkiss AK, Rider CV, Gray LE Jr. Diverse mechanisms of anti-androgen action: impact on male rat reproductive tract development. Int J Androl. 2008; 31:178–187. [PubMed: 18315717]

Wong VC, Hui SL. Epidemiological study of autism spectrum disorder in China. J Child Neurol. 2008; 23:67–72. [PubMed: 18160559]

Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Prevalence of autism in a US metropolitan area. Jama. 2003; 289:49–55. [PubMed: 12503976]

Author Agreement Form

I the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

I confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

I understand that the Corresponding Author is the sole contact for the Editorial process. He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

Signed by the corresponding author: Bernard Weiss

Implications and Conclusions

Our findings, and the questions they evoke, may be listed as follows:

Phthalate exposure early in development appears linked to ASD.

Is the link due to its association with allergies and asthma? Is it an independent factor, acting perhaps via endocrine disruption? Or is it a confounding phenomenon not yet identified? Biomarkers such as urinary metabolites would be a useful source of answers.

Other indoor environmental variables, such as dampness, are also linked to ASD.

Is ventilation rate in the home an effect modifier?

Is economic stress a risk factor for ASD or simply a reflection of altered family circumstances arising from an ASD child in the home?

What are some potential mechanisms for the connection between indoor environmental variables and ASD?

In this study, we did not expect, or even intend to search for, an association between PVC flooring and ASD. The study was not designed specifically to address ASDs, and confirmation would require further efforts. Nevertheless, we believe the data warrant publication at this time because, so far, we lack confirmed environmental contributions to the etiology of autism despite considerable searching.

Figure 1.
Location of the county of Värmland, Sweden.

Table 1
Description of 4,779 children, their families and the homes

Factor	Frequency n (%)		Trends[3]
Year	Questionnaire 2000 (Baseline)	Questionnaire 2005 (Follow up)	
Age of the child (y)			
6	-	1557 (32.6)	
7	-	1568 (32.8)	
8	-	1654 (34.6)	
Type of building			
Single family house	3871 (81)	4090 (85.6)	Increased
Multi family house	793 (16.6)	546 (11.4)	Decreased
Size of the home (m^2)			
<75	326 (6.8)	135 (2.8)	Decreased
75-150	3389 (70.9)	3240 (67.8)	
>150	1013 (21.2)	1332 (27.9)	Increased
Flooring material in the child's bedroom			
PVC	2360 (51.9)	1858 (40.3)	Decreased
Wood	1565 (34.4)	2155 (46.8)	Increased
Linoleum	364 (8.0)	341 (7.4)	
Flooring material in the parent's bedroom			
PVC	2067 (44.8)	1584 (33.6)	Decreased
Wood	1922 (41.7)	2497 (54.4)	Increased
Linoleum	326 (7.1)	285 (6.2)	
Condensation on inside of windows in[1]:			
Childs room No	3197 (66.9)	3305 (69.2)	
1-5 cm	811 (17.0)	923 (19.3)	
> 5 cm	446 (9.3)	363 (7.6)	Decreased
Parents room No	2970 (62.1)	3147 (65.9)	
1-5 cm	941 (19.7)	1032 (21.6)	
> 5 cm	616 (12.9)	419 (8.8)	Decreased
Living room No	3586 (75.0)	3870 (81.0)	
1-5 cm	595 (12.5)	518 (10.8)	
> 5 cm	286 (6.0)	174 (3.6)	Decreased
Divorce[2]			
Yes	324 (6.8)	960 (20.1)	
Economical problems[3]			
No	-	4174 (87.3)	
Yes	-	537 (11.2)	
No reply	-	68 (1.4)	

Factor	Frequency n (%)		Trends[3]
Allergy in family			
No	2167 (45.3)	-	
Yes	2563 (53.6)	-	
Smoking in family			
Any smoker	1044 (21.8)	909 (19.0)	
Smoking mother	673 (14.1)	605 (12.7)	Decreased
Smoking father	497 (10.4)	398 (8.3)	Decreased

1) Condensation on the inside of the windows during heating season.

2) In 2000 there was no question on divorce but on how many adults that normally lived in the home (1, 2, 3 or more). In 2005 there was a question on if the child lived with both biological parents (Yes vs. No)

3) Have your family had problems with paying bills during the last 12 months.

4) Indicated trends during the five year period.

Table 2

ASD among children 2005 and associated background factors

Factor 2000	**ASD n (%)**			**p-value**	
				Chi-2	Trend[1]
Sex	boys	girls			
	60 (2.5)	12 (0.5)		**0.001**	
Age (y)	6	7	8		
	18 (1.2)	23 (1.5)	31 (1.9)		0.092
No. of children less than 7 years in family	1	2	3 or more		
	40 (1.9)	30 (1.3)	1 (0.3)		**0.031**

1) Linear-by-linear association

Table 3

Crude associations between factors that could be a proxy for socioeconomic status and ASD five years later for 4,779 children.

Factor (2000)	**ASD**					
	Reference		**OR (95% CI)**			
Type of building	**n (%)**	*SH*	**n (%)**	*MH*	**n (%)**	
2000	52 (1.3)	1.0	15 (1.9)	1.42 (0.80-2.53)		
2005	55 (1.3)	1.0	13 (2.4)	1.79 (0.97-3.29)		
Size of the home (m^2)		*>150*		*75-150*		*<75*
2000	11 (1.1)	1.0	54 (1.6)	1.47 (0.77-2.83)	6 (1.8)	1.70 (0.62-4.63)
2005	14 (1.1)	1.0	52 (1.6)	1.54 (0.85-2.78)	3 (2.2)	2.15 (0.61-7.58)
Divorce[2]		*No*		*Yes*		
2000	61 (1.4)	1.0	10 (3.1)	**2.22 (1.13-4.37)**		
2005	43 (1.1)	1.0	28 (2.9)	**2.62 (1.62-4.24)**		
Economical problem[3] **2005**		*No*		*Yes*		
	51 (1.2)		20 (3.7)	**3.11 (1.84-5.27)**		
Smoking in family		*No*		*Yes*		
Any smoker in family	51 (1.4)	1.0	21 (2.0)	1.49 (0.89-2.48)		
Smoking mother	54 (1.3)	1.0	18 (2.7)	**2.06 (1.20-3.53)**		
Smoking father	60 (1.4)	1.0	12 (2.4)	1.75 (0.94-3.28)		
Smoking during first year		*No*		*Yes, but stopped*		*Yes*
Mother	56 (1.4)	1.0	1 (1.9)	1.37 (0.19-10.08)	15 (2.9)	**2.09 (1.17-3.72)**
Father	51 (1.4)	1.0	2 (3.3)	2.47 (0.59-10.39)	12 (2.2)	1.66 (0.88-3.13)
Smoking during pregnancy		*No*		*Yes, but stopped*		*Yes*
Mother	55 (1.4)	1.0	6 (2.3)	1.62 (0.69-3.80)	11 (2.9)	**2.09 (1.08-4.03)**
Father	50 (1.3)	1.0	1 (2.0)	1.47 (0.20-10.86)	13 (2.3)	1.73 (0.93-3.20)
Any smoking in mother[4]		*No*		*Yes*		
	51 (1.4)	1.0	21 (2.4)	**1.76 (1.05-2.94)**		
Smoking in family 2005		*No*		*Yes*		
Any smoker in family	52 (1.4)	1.0	20 (2.2)	1.64 (0.98-2.76)		

Factor (2000)	ASD					
	Reference		OR (95% CI)			
Smoking mother	57 (1.4)	1.0	15 (2.5)	**1.82 (1.02-3.24)**		
Smoking father	63 (1.5)	1.0	9 (2.3)	1.58 (0.78-3.21)		

1) Trends in data estimated with linear by linear associations (p<0,05).

2) In 2000 there was no question on divorce but on how many adults that normally lived in the home (1, 2, 3 or more). In 2005 there was a question on if the child lived with both biological parents (Yes vs. No).

3) Have your family had problems with paying bills during the last 12 months.

4) Any mother smoking (current smoking, during pregnancy and/or during child's first year).

Table 4

Association between allergic symptoms in the child 2000 and ASD five year later among 4,779 children.

Allergic symptoms	**Follow up study 2005 (6y, 7y, 8y)**				
Baseline (2000)	**ASD (%)**		**p-value[1]**	**OR (95 % CI)**	**AOR[2] (95 % CI)**
	No	Yes			
	n=4,689	n=72			
Wheezing ever	24.9	37.5	**0.014**	**1.81 (1.12-2.93)**	1.46 (0.89-2.38)
Cough at night	7.3	12.7	0.083	1.85 (0.91-3.76)	1.72 (0.84-3.52)
Doctor diagnosed asthma	5.2	11.3	**0.022**	**2.33 (1.10-4.92)**	1.75 (0.82-3.75)
Rhinitis ever	12.0	16.9	0.213	1.49 (0.79-2.78)	1.23 (0.65-2.33)
Allergic rhinitis	1.4	1.4	0.990	1.01 (0.14-7.41)	0.78 (0.11-5.77)
Eczema ever	21.9	25.0	0.535	1.19 (0.69-2.03)	1.08 (0.63-1.87)
Follow up (2005)	No	Yes	**p-value[1]**	**OR (95 % CI)**	**AOR[2] (95 % CI)**
	n=4,689	n=72			
Wheezing ever	24.0	38.0	**0.006**	**1.94 (1.20-3.15)**	1.50 (0.91-2.46)
Cough at night	6.2	8.5	0.442	1.39 (0.60-3.24)	1.24 (0.53-2.92)
Doctor diagnosed asthma	8.5	19.4	**0.001**	**2.59 (1.43-4.68)**	**1.88 (1.02-3.45)**
Rhinitis ever	20.4	29.2	0.067	1.61 (0.96-2.69)	1.31 (0.78-2.23)
Allergic rhinitis	6.3	8.3	0.483	1.35 (0.58-3.14)	1.03 (0.44-2.42)
Eczema ever	23.2	31.9	0.081	1.56 (0.94-2.57)	1.60 (0.96-2.67)

1) Chi square test.

2) Adjustment made for allergic symptoms in family in the year of 2000, sex and any smoking in mother (current smoking, during pregnancy and/or during child's first year)

Table 5

Association between allergic symptoms in family 2000 and parental reported ASD in the child at the follow up 2005.

Allergic symptoms in family 2000	**ASD 2005**		
	(%)		**p-value**[1]
Allergic symptoms in family	No	Yes	
Any symptoms in family[2]	1.3	1.8	0.154
Mother			
Asthma	1.4	2.3	0.187
Rhinitis	1.4	1.9	0.258
Eczema	1.4	2.5	**0.023**
Father			
Asthma	1.6	0.6	0.138
Rhinitis	1.5	1.7	0.534
Eczema	1.5	1.5	0.959

1) Chi square test

2) Asthma, rhinitis or eczema in father, mother or siblings

Table 6

Associations between self reported SBS (Sick Building Syndrome) symptoms among parents 2000 and ASD among their children five years later

SBS Symptom 2000[1]	ASD n (%)			p-value[2]
	Yes, often	Yes, sometimes	No, never	
Tiredness (29.3, 57.4)	26 (1.9)	40 (1.5)	5 (0.9)	0.100
Heavy head (7.5, 47.9)	5 (1.4)	40 (1.8)	26 (1.3)	0.461
Headache (10.2, 63.4)	11 (2.3)	46 (1.5)	14 (1.2)	0.118
Dizziness (2.9, 21.3)	2 (1.4)	22 (2.2)	46 (1.3)	0.125
Concentration difficulties (2.7, 23.3)	4 (3.1)	26 (2.3)	41 (1.2)	**0.003**
Irritation in eyes (2.2, 17.5)	7 (6.8)	17 (2.0)	47 (1.3)	**0.001**
Irritation in nose (4.8, 36.3)	5 (2.2)	30 (1.7)	36 (1.3)	0.191
Hoarseness (1.6, 18.7)	2 (2.7)	18 (2.0)	51 (1.4)	0.117
Cough (2.1, 30.0)	-	29 (2.0)	42 (1.4)	0.357
Skin problem face (5.2, 17.0)	9 (3.6)	18 (2.2)	44 (1.2)	**0.001**
Skin problem head (5.3, 13.2)	8 (3.2)	11 (1.8)	52 (1.4)	**0.035**
Skin problem hands (11.2, 23.3)	7 (1.3)	21 (1.9)	43 (1.4)	0.751

1) SBS symptoms among parents 2000 with prevalence in parenthesis (Yes often (%), Yes sometimes (%)).

2) Linear-by-linear association.

Neurotoxicology. Author manuscript; available in PMC 2013 October 01.

Table 7

Association between home environmental factors and ASD among children aged 6-8 years old.

Factor	**ASD**					
	Reference			**OR (95% CI)**		
Flooring material	**n (%)**		**n (%)**		**n (%)**	
Child's room		*All other*		*PVC*		
	25 (1.2)	1.0	41 (1.7)	1.42 (0.86-2.34)		
		Wood/Linoleum		*PVC*		
	24 (1.2)	1.0	41 (1.7)	1.41 (0.85-2.33)		
		Wood		*PVC*		
	14 (0.9)	1.0	41 (1.7)	**1.96 (1.07-3.61)**		
Parent's room		*All other*		*PVC*		
	28 (1.2)	1.0	40 (1.9)	**1.66 (1.02-2.70)**		
		Wood/Linoleum		*PVC*		
	24 (1.1)	1.0	40 (1.9)	**1.83 (1.10-3.05)**		
		Wood		*PVC*		
	15 (0.8)	1.0	40 (1.9)	**2.51 (1.38-4.57)**		
Flooring material 2005						
		All other		*PVC*		
Child's room	34 (1.3)	1.0	29 (1.9)	1.46 (0.88-2.40)		
Parent's room	36 (1.3)	1.0	31 (2.0)	1.61 (0.99-2.61)		
Condensation						
		No		*1-5 cm*		*>5 cm*
Child's room	41 (1.3)	1.0	13 (1.6)	1.26 (0.67-2.36)	12 (2.7)	**2.13 (1.11-4.08)**[1]
Parent's room	38 (1.3)	1.0	17 (1.8)	1.42 (0.80-2.53)	16 (2.6)	**2.06 (1.14-3.71)**[1]
Living room	47 (1.3)	1.0	10 (1.7)	1.29 (0.65-2.57)	9 (3.2)	**2.45 (1.19-5.05)**[1]
Condensation 2005[2]						
		No		*1-5 cm*		*>5 cm*
Child's room	42 (1.3)	1.0	17 (1.8)	1.46 (0.83-2.58)	12 (3.3)	**2.67 (1.39-5.13)**[1]

Factor	ASD					
	Reference			OR (95% CI)		
Parent's room	38 (1.2)	1.0	21 (2.0)	1.70 (0.99-2.91)	12 (2.9)	**2.43 (1.26-4.68)**[1]
Living room	52 (1.3)	1.0	10 (1.9)	1.45 (0.73-2.88)	9 (5.2)	**4.00 (1.94-8.25)**[1]

[1)] Trends in data estimated with linear by linear associations (p<0,05).

[2)] Condensation on the inside of the windows during winter time

Table 8

Adjusted associations between different factors and ASD in six different models regarding type of flooring in the bedrooms of the home (I-VI).

Factor 2000	**OR (95% CI)**					
	Child's bedroom			**Parent's bedroom**		
Model	I	II	III	IV	V	VI
Flooring material						
PVC vs. all other material	1.19 (0.71-2.00)	-	-	1.59 (0.97-2.61)	-	-
PVC vs. Wood/Linoleum	-	1.19 (0.70-2.02)	-	-	**1.74 (1.04-2.92)**	-
PVC vs. Wood	-	-	1.59 (0.85-2.99)	-	-	**2.40 (1.31-4.40)**
Condensation on windows[1]						
No	1.0	1.0	1.0	1.0	1.0	1.0
1-5 cm	1.35 (0.71-2.57)	1.39 (0.73-2.64)	1.24 (0.60-2.57)	1.52 (0.84-2.73)	1.36 (0.74-2.53)	1.49 (0.76-2.91)
>5 cm	**2.05 (1.03-4.10)**	**2.13 (1.06-4.25)**	**2.27 (1.09-4.74)**	**2.03 (1.08-3.82)**	**1.93 (1.01-3.70)**	**2.40 (1.22-4.71)**
Mother smoking[2]	**1.79 (1.02-3.13)**	1.66 (0.94-2.94)	1.63 (0.87-3.04)	1.51 (0.87-2.62)	1.53 (0.87-2.69)	1.42 (0.76-2.64)
Age						
6	1.0	1.0	1.0	1.0	1.0	1.0
7	1.03 (0.53-2.00)	1.02 (0.53-1.99)	1.16 (0.54-2.48)	1.13 (0.60-2.13)	1.07 (0.56-2.03)	1.31 (0.64-2.68)
8	1.37 (0.73-2.55)	1.31 (0.70-2.46)	1.63 (0.80-3.32)	1.41 (0.77-2.58)	1.24 (0.67-2.30)	1.54 (0.77-3.09)
Sex (boys)	**5.53 (2.69-10.56)**	**5.89 (2.88-12.03)**	**4.77 (2.30-9.89)**	**5.38 (2.80-10.33)**	**5.56 (2.81-11.01)**	**4.67 (2.33-9.37)**
Asthma in the child	1.73 (0.77-3.91)	1.74 (0.77-3.93)	1.72 (0.71-4.16)	1.91 (0.89-4.10)	2.04 (0.95-4.40)	2.09 (0.92-4.76)
Financial problems 2005[3]						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	**2.48 (1.34-4.60)**	**2.58 (1.39-4.79)**	**3.02 (1.57-5.82)**	**3.00 (1.69-5.33)**	**2.81 (1.54-5.13)**	**3.18 (1.68-6.00)**
No reply	1.49 (0.20-11.21)	1.58 (0.21-11.93)	2.04 (0.27-15.60)	1.38 (0.18-10.35)	1.40 (0.19-10.54)	1.94 (0.25-14.84)

*1)*Condensation on the inside of the windows in child's room during heating season.

*2)*Any mother smoking (current smoking, during pregnancy and/or during child's first year).

*3)*Have your family had problems with paying bills during the last 12 months.