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# ARE PARENTS OF AD/HD CHILDREN MORE SUSCEPTIBLE TO ENVIRONMENTAL EXPOSURES THAN CONTROLS?

## JUSTIFICATION

Exposure to neurotoxins is generally insidious. People often are unaware of what exposures they have encountered. Despite the widespread home and commercial use of pesticides, we know very little about their damaging effects upon a fetus. This stands in stark contrast to our knowledge of the adverse effects of heavy metals, PCBs and other substances that are stored in human tissues. It is far simpler to correlate cognitive problems and adverse birth outcomes to an exposure like lead that can be measured through a biological sample (e.g., blood or teeth). In the case of organophosphates and newer pesticides, damage may occur at varying stage(s) of fetal development, depending upon when exposure occurs. Soon after exposure, these toxicants are excreted, making it impossible to identify or quantify past exposures. Their silent passage through the fetal nervous system may later manifest as attention and neurobehavioral deficits or the myriad learning, mental, and motor disabilities associated with AD/HD.

Recently, it has become evident that specific genetic polymorphisms can affect individuals' ability to detoxify environmental chemicals and that the polymorphisms they inherit can serve as underlying risk factors for neurological impairment. Thus, not everyone who is exposed to an environmental toxicant may become impaired—only the subset of individuals who are genetically pre-disposed. Specific genetic polymorphisms, including PON-1, CYP2D6 and NAT2, have been shown to underlie chemical intolerance—the inability to tolerate a wide variety of structurally unrelated environmental chemicals. The vast majority of individuals who develop chemical intolerances following a well-defined exposure, such as home remodeling or pesticide application, subsequently report a wide array of neurological problems, most notably attention, learning and memory difficulties—symptoms that mimic AD/HD. The term "toxicant-induced loss of tolerance" (TILT) has been used to describe this phenomenon. Researchers in more than a dozen countries have observed a correlation between environmental exposure and the development of chemical intolerances in demographically diverse populations (see diagram below).

The prevalence of learning and behavioral disabilities is rising so quickly that many health professionals refer to it as "epidemic." The prevalence of AD/HD is reported as 3 to 5% of school-aged children, but a recent study suggests its prevalence may be as high as 10%. The broad spectrum of motor deficits and learning, behavioral, and psychological disorders commonly associated with the AD/HD diagnosis further increase its public health impact. The chart below illustrates the burden imposed on families and the health care and educational systems. Children with AD/HD encounter difficulties in all areas of their lives, including high school completion, finding jobs, and social interactions.

Co-morbid Disorders	Prevalence
Motor Coordination Disorders	50%
Learning Disabilities	up to 50%
Disruptive Behavior Disorders	
Conduct Disorder	25%
Oppositional Defiant Disorder	40%
Mood Disorders	
Depression	10-30%
Bipolar Disorder	20%
Anxiety Disorders	30%
Tourette's Syndrome	7%
Autism	(association)
Asperger's Syndrome	(association)
Physical Anomalies	(association)
Wide-set eyes	
Highly arched palate	
Low-set ears	

### Exposures That May Initiate TILT or Trigger Symptoms



## STUDY PLAN

This study attempts to circumvent the difficulty in quantifying past exposures by going through the "back door", i.e., by evaluating parents of AD/HD children to determine whether they are more chemically intolerant than parents of non-AD/HD children. We propose a case-control study to compare the prevalence of chemical intolerance in parents of AD/HD children with that of parents whose children do not manifest AD/HD. To accomplish this, we will use a secured computer-based survey to collect parent and child exposure histories. The survey will include a validated instrument that has been widely used in various populations to assess chemical intolerance and will provide individual chemical intolerance scores. The exposure history will include questions concerning chemical and pesticide use, occupational exposures, residential proximity to industrial sites, and timing of exposures in relation to pregnancy. The use of a national online survey to collect exposure data in this manner is a novel approach, one that provides access to a large national sample of cases and controls, thus increasing statistical power and the potential to identify significant risk factors for this debilitating disorder.

## HYPOTHESES

Parents of AD/HD children will have higher mean chemical intolerance scores than matched controls.

Children born to parents with higher chemical intolerance scores will have a higher prevalence of co-morbid mental, learning/behavioral, and motor coordination disorders than matched controls.



## REFERENCES

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## METHODS AND DATA COLLECTION

### Recruitment

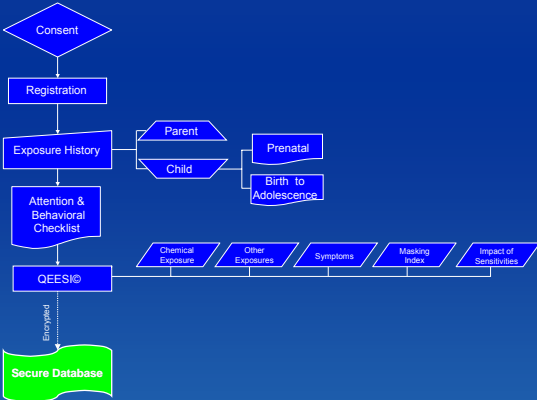
Parents will be recruited through national AD/HD organizations, advertisements in physicians' newsletters, patient groups' newsletters, conference proceedings, flyers, and newspaper ads.

Cases: parents of children three years of age or older who have physician-diagnosed AD/HD ( $n = 150$ ).  
Controls: parents of children three years of age or older who do not have an AD/HD diagnosis ( $n = 150$ ).

### Study Design

The following steps describe the process participants will follow as they navigate through the website and survey (see flow chart below).

- Step 1** Information regarding the project's purpose, use of data, and protection of privacy is provided on the electronic consent page.
- Step 2** Once participants complete and submit the registration page, a PIN number is generated, allowing participants to complete the survey at their convenience.
- Step 3** Participants are then directed to the family history questionnaire. The questionnaire is a comprehensive survey of parental exposures, pre- and post-natal exposures, childhood exposures, and co-morbid disorders associated with AD/HD.
- Step 4** The American Psychiatric Association's (APA) criteria for attention and behavior disorders follows the exposure history and are included as a screening tool. To qualify as a case, a parent's child must have physician-diagnosed AD/HD and meet at least one of these APA criteria.
- Step 5** The Quick Environmental Exposure and Sensitivity Inventory (QEESt) will be used to score chemical intolerance.
- Step 6** Each survey will be stored in a database, identified only by a confidential PIN number. Survey data will be encrypted and secured with appropriate electronic measures at the University's Computer Resource Department.



## ANALYSIS

The Chemical Intolerance and Other Intolerance scales from the QEESt will provide a measure of each individual's overall intolerance. Criteria for assessing intolerance scale scores will be taken from published, validated studies. T-tests will be used to compare the intolerance scores for controls and cases. A sample of 300 subjects achieves 81% power to detect an odds ratio of 2.00 versus the alternative of equal odds using a chi-square test with a 0.05 significance level. Chi-square tests will determine whether an association exists between parents with high intolerance scores and the incidence of the following: mental disorders, learning disabilities, and behavioral disabilities, as well as all co-morbid disorders combined. Criteria for high sensitivity is  $\geq 40$  and low sensitivity is  $\leq 20$ , respectively. The tests will be conducted at the  $\alpha = 0.05$  level of significance. Where significant associations exist, odds ratios will be calculated to determine the strength of association.

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This fellow is sponsored by EPA's STAR or Greater Research Opportunities (GRO) Program.