ADHD and Adverse Health Outcomes in Adults

Thomas J. Spencer, MD

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## Disclosures

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<tr>
<th>Company</th>
<th>Role/Support</th>
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<tr>
<td>FDA</td>
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<td>Department of Defense</td>
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<td>Sunovion</td>
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Dr. Spencer receives research support from Royalties and Licensing fees on copyrighted ADHD scales through MGH Corporate Sponsored Research and Licensing.

Dr. Spencer has a US Patent Application pending (Provisional Number 61/233. 686), through MGH corporate licensing, on a method to prevent stimulant abuse.
ADHD, Cognitive Deficits

Unhealthy Lifestyle

Established Risk Indicators

DISEASE
Aims of the study:

The aims of our study were to examine whether ADHD is associated with

1) adverse health habits and 2) objective and subjective adverse health risk indicators relative to age and sex matched Controls.

We examined the relationship between adverse health habits and adverse health risk indicators
We ascertained a sample of 100 untreated ADHD adults and 100 non-ADHD adults of similar age and sex to quantify the risk for unhealthy lifestyle and adverse health risk indicators.

We hypothesized that ADHD would be associated with a higher risks for both an unhealthy lifestyle and adverse health risk indicators.
ADHD and Adverse Health Outcomes in Adults

Spencer, Biederman et al. 2014

Methods

Subjects

Adults between 18 and 60 years of both sexes.

ADHD subjects not treated for greater than one month. Control subjects no more than two symptoms of ADHD.

Exclusion criteria included deafness, blindness, psychosis, inadequate command of the English language, and a full-scale IQ less than 80.
Methods

Health Habits Assessments

The Behavioral Risk Factor Surveillance System (BRFSS) was established in 1984 by the Centers for Disease Control and Prevention (CDC), the BRFSS collects information on health risk behaviors, preventive health practices, and health care access.

From the BRFSS we used the following items: a personal doctor/health care provider, a healthy diet (fruits and vegetables), exercise, cigarette smoking, alcohol use, risky sex, health care coverage, frequency of visits to primary care physicians and dental providers, and flu shots.

This information is related to conditions linked to leading causes of death—heart disease, cancer, stroke, diabetes, and injury—and other important health issues.
Health Risk Indicators Assessments

*Questionnaires* assessing self-rated health history of diabetes, heart attacks, asthma, limits in activities due to physical, mental, or emotional problems, need to use special equipment, musculoskeletal complaints (joint pain/aching/stiffness), and history of arthritis, rheumatoid arthritis (RA), gout, lupus, and fibromyalgia.
Health Risk Indicators Assessments

*Objective measures* of adverse health risk indicators included measurements of serum lipid profiles (cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides), glucose and levels of C-reactive protein (CRP). In addition, we obtained ECGs and measured vital signs (first and second systolic, diastolic BP, pulse), weight, height, BMI and waist circumference.

We measured urine nicotine and urine cotinine.
ADHD and Adverse Health Outcomes in Adults

Spencer, Biederman et al. 2014

Statistical Methods

For health risk indicators, cutoffs were defined as “bad” or “worse”

Bad outcomes cutoffs were defined by values in the high end of normal, while worse outcome cutoffs were set at values outside the normal range.

Univariate associations were evaluated using chi-squared tests for categorical variables and t-tests for continuous variables, as indicated.

Tallied outcomes (total habits, total outcomes) were evaluated with a Poisson model, and group by age interactions were evaluated by adding an interaction term to the Poisson model.
# Table 1. Demographics for the Health Outcomes Dataset, stratified by ADHD status

<table>
<thead>
<tr>
<th></th>
<th>ADHD n=98</th>
<th>Control n=100</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32±12</td>
<td>30±10</td>
<td>t=1.14</td>
<td>0.26</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>43 (44%)</td>
<td>47 (47%)</td>
<td>χ²(1)=0.19</td>
<td>0.66</td>
</tr>
<tr>
<td>Race (Caucasian)</td>
<td>82 (85%)*</td>
<td>80 (80%)</td>
<td>χ²(1)=0.69</td>
<td>0.41</td>
</tr>
<tr>
<td>Socioeconomic status (SES)</td>
<td>2.10±0.88**</td>
<td>1.99±0.87***</td>
<td>t=0.92</td>
<td>0.36</td>
</tr>
</tbody>
</table>

All values in table represent mean±S.D. or frequency (%)

*1 missing **5 missing ***8 missing
Mean Number of “Bad” Habits

Spencer, Biederman et al. 2014
Health Habits

Spencer, Biederman et al. 2014

<table>
<thead>
<tr>
<th>Health Habit</th>
<th>ADHD (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Personal Doctor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Doctor Visit &gt; 2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Health Coverage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No flu shot Last year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Health Habits

Spencer, Biederman et al. 2014

Limited Fruits and Vegetables  Not do Mod Activity >10 min  No Phys Activ Outside of Work

All NS
Health Habits

Spencer, Biederman et al. 2014

Epilepsy in last 30 days
Risky drug use
Risky sex
Smoked >100 cig
Urine Nicotine Cotinine

ADHD
Control
All NS
Mean number of Adverse Health Risk Indicators

“Bad” Health Risk Indicators

N=137
p=0.005

Spencer, Biederman et al. 2014
Mean number of Adverse Health Risk Indicators

“Worse” Health Risk Indicators

Spencer, Biederman et al. 2014

N=137
p=0.003

Mean Number of Worse Adverse Health Risk Indicators

ADHD

Control

Spencer, Biederman et al. 2014
RESULTS

Further examination of individual health risk indicators outcomes showed that ADHD subjects had worse individual health outcomes than Controls in lipid profiles (LDL>160, p=0.026), diastolic BP (>90, p=0.042), BMI (>25, p=0.022), asthma (p=0.003), musculoskeletal complaints (joint pain/aching/stiffness, p=0.031), and arthritis/RA/gout/lupus/fibromyalgia (p=0.044).

Although worse in ADHD subjects than Controls, self-assessment of overall health just missed statistical significance (p=0.051).
Adverse Health Risk Indicators

Lipids and Glucose

Spencer, Biederman et al. 2014

* p<0.05

- Triglycerides: >200
- Cholesterol: >250
- HDL: <40
- LDL: >160
- Cardiac Risk: >5
- Glucose: >115
Adverse Health Risk Indicators

Vital Signs

Spencer, Biederman et al. 2014

*p<0.05

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Systolic BP &gt;140</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Diasystolic BP &gt;100</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Systolic BP &gt;140</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Diasystolic BP &gt;90</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Pulse &gt;100</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>EKG HR &gt;100</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>
“Bad” Adverse Health Risk Indicators

Weight, Inflammation

Spencer, Biederman et al. 2014

BMI
>25

Waist/Hgt
>50%

Inflammation
CRP >3

* p<0.05
Health Outcomes

Spencer, Biederman et al. 2014

- ** p<0.005
- * p<0.05
- p<0.051

Bar chart showing differences in health outcomes between ADHD and control groups for various conditions:

- Self Rated Health
- Asthma
- Limited Activities
- Joint Pain
- Arthritis
Adjusted Predictions of Interaction between ADHD Status and Age

Number of “Worse” Adverse Health Risk Indicators
Main Findings

No meaningful differences between ADHD subjects and Controls were identified either in the omnibus aggregate of health habits or in individual health habits in an (average) 32 year old sample.

Robust differences were identified in aggregate measures of both borderline and frankly abnormal adverse health outcome indicators.

While the interaction with age was not statistically significant, aggregate scores on both “bad” and “worse” outcomes nominally diverged in the older age group.
Comment

Adverse Health Habits

Barkley et al. clinically referred adults with ADHD vs. controls

Similar to our findings Barkley reported no meaningful differences in nutrition and eating habits, caffeine use, physical activity, alcohol use, and risky sexual activities.

Dissimilar to our findings Barkley et al. reported differences in sleep habits, tobacco use, non-medical drug use, and the frequency of medical/dental care.
Comment

Adverse Health Habits

Barkley et al. longitudinal study of ADHD children followed into adulthood.

Also dissimilar to our study Barkley et al. reported ADHD subjects differed from controls on eating habits, sleep, tobacco use, and non-medical drug use.

While these differences could be accounted for by methodological differences between the studies, more work is needed to help reconcile these differences.
Effect of drugs on the risk of injuries in children with ADHD: a prospective cohort study

Søren Dalsgaard et al. Lancet Psychiatry 2015

Prevalence of injuries in children without ADHD (n=705 563) and by pharmacological treatment status in children with ADHD (n=4557). Treatment was defined as pharmacological treatment for at least 6 months during a year after age 5 years and before age 10...
Comment

Adverse Health Indicators

Barkley et al. longitudinal study of ADHD children followed into adulthood.

They found greater BMI (like our study) and HDL (we did not)

Unlike our study, they failed to find differences in BP, LDL.

The Milwaukee sample was younger age (27 years) and partially (40%) treated with stimulants
Comment

Adverse Health Indicators

Our findings of increased BMI are consistent with a meta-analysis in unmedicated individuals with ADHD. ((Cortese AJP 2016)

Finally, a longitudinal population study of 15,197 adolescents reported that self-reported ADHD symptoms at baseline correlated with adult BMI, which, accounted for hypertension at the 14 year follow up. (Fuemmeler et al. 2011)
Association Between ADHD and Obesity for Unmedicated Individuals With ADHD

Cortese et al. AJP 2016

<table>
<thead>
<tr>
<th>Study</th>
<th>ADHD (N)</th>
<th>Comparison Subjects (N)</th>
<th>Odds Ratio (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Byrd (41)</td>
<td>227</td>
<td>2638</td>
<td>1.23 (0.88, 1.71)</td>
<td>11.56</td>
</tr>
<tr>
<td>Curtin (43)</td>
<td>66</td>
<td>8276</td>
<td>1.54 (0.86, 2.75)</td>
<td>5.44</td>
</tr>
<tr>
<td>Dubnov-Raz (13)</td>
<td>140</td>
<td>51</td>
<td>0.32 (0.11, 0.92)</td>
<td>1.91</td>
</tr>
<tr>
<td>Hanc (47)</td>
<td>140</td>
<td>396</td>
<td>0.76 (0.30, 1.92)</td>
<td>2.45</td>
</tr>
<tr>
<td>Kim (52)</td>
<td>2490</td>
<td>60573</td>
<td>1.34 (1.14, 1.57)</td>
<td>19.87</td>
</tr>
<tr>
<td>Lingineni (54)</td>
<td>1292</td>
<td>38510</td>
<td>1.56 (1.36, 1.80)</td>
<td>21.00</td>
</tr>
<tr>
<td>Phillips (57)</td>
<td>230</td>
<td>8141</td>
<td>1.89 (1.38, 2.60)</td>
<td>12.17</td>
</tr>
<tr>
<td>Poulton (58)</td>
<td>34</td>
<td>241</td>
<td>3.88 (1.10, 13.67)</td>
<td>1.39</td>
</tr>
<tr>
<td>Poulton (59)</td>
<td>65</td>
<td>174</td>
<td>0.89 (0.18, 4.41)</td>
<td>0.88</td>
</tr>
<tr>
<td>Spencer (9)</td>
<td>66</td>
<td>100</td>
<td>3.09 (1.21, 7.86)</td>
<td>2.41</td>
</tr>
<tr>
<td>Waring (10)</td>
<td>2431</td>
<td>57204</td>
<td>1.35 (1.12, 1.62)</td>
<td>18.59</td>
</tr>
<tr>
<td>Wilhelm (63)</td>
<td>31</td>
<td>48</td>
<td>1.53 (0.59, 3.98)</td>
<td>2.33</td>
</tr>
<tr>
<td>Overall (I²=48.0%, p=0.032)</td>
<td></td>
<td></td>
<td>1.43 (1.23, 1.67)</td>
<td>100.00</td>
</tr>
</tbody>
</table>
ADHD and Adverse Health Outcomes in Adults

Spencer, Biederman et al. 2014

Comment

Our results suggest that the relationship between ADHD and adverse medical risks is not mediated by the abnormal health habits assessed in our study.

The pathophysiology of ADHD may have a direct influence on health risk indicators.

For example, immune system abnormalities have been implicated in ADHD and a well-validated rat model of ADHD also develops hypertension.

Additional work is needed to investigate the mechanisms by which ADHD confers to the affected individual an increased medical risk and whether such risks can be mitigated by treatment.
Comment

Limitations

While we used a standardized survey system it is possible that the questionnaires are worded in a way that is not sensitive to identifying differences in this population.

Differences in health behaviors and adverse health risk indicators may be subtle at the relatively young age of our sample (mean 32).

We did not address the effect of treatment on health behaviors and adverse health risk indicators.
Comment

Limitations

Our finding that tobacco use was not increased in our ADHD sample is not consistent with previous studies that documented that ADHD significantly increases the risk for smoking. This could suggest that our ADHD sample is atypically healthy, which could account for our failure to find group differences in health behaviors.

Because the sample was largely Caucasian, it may not generalize to other ethnic groups.
Conclusions

Our results confirm that ADHD is associated with an adverse impact in physical health.

They failed to support the hypothesis that the etiology of these outcomes is driven by differences in health habits.

Our work suggests that ADHD is a risk factor for adverse medical outcomes, medical morbidity and, perhaps, premature death.
Conclusions

It is unknown whether early identification and treatment of ADHD may modify adverse health outcomes.

The study highlights the importance of screening adults with ADHD for comorbid medical disorders, such as obesity or hyperlipidemia, and insuring concurrent treatment (i.e., exercise, statins).

Adults with ADHD symptoms are a medically complex group with a variety of problems besides ADHD often necessitating close collaboration with their PCP.