The Biological Basis of Autism: Causation & Treatment

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• "Therefore, to examine the autism as mercury poisoning hypothesis, this paper reviews the existing scientific literature within the context of established epidemiological criteria and finds that the evidence for a causal relationship is compelling."

• "Analogous to epidemiological evidence of the smoking–lung cancer relationship, a mercury–autism relationship is confirmed."

• "Therefore, given the severity, devastating lifelong impact and extremely high prevalence of autism, it would be negligent to continue to expose pregnant and nursing mothers and infant children to any amount of avoidable mercury."

Low Glutathione & Sulfate in Autistic Disorders

** Mercury Excretion is Directly Related to Glutathione Secretion

**Observed that female hormones afforded total protection against Thimerosal toxicity.**

**Observed testosterone at 1.0 micromolar levels that by itself did not significantly increase neuron death (red flattened oval), within 3 hours when added with 50 nanomolar Thimerosal (solid circles) caused 100% neuron death. [Fifty nanomolar Thimerosal at this time point did not significantly cause any cell death.]**


The authors examined 72 children with autism, including 23 children with Asperger syndrome, 34 siblings, 88 fathers, 88 mothers, and sex and age-matched controls. The authors demonstrated that the more severely affected the children were the higher the levels of prenatal testosterone.

Steroidogenic Pathway:
Hyperandrogenicity in Children with Neurodevelopmental Disorders:
Potential Insights into Testosterone Levels & Potential Testosterone Adverse Effects

Am J Psychiatry 1997;154:1626-7

Androgenic Activity in Autism
Sylvie Tordman, M.D., Ph.D., Pierre Perrard, M.D., Veronique Sutlom, M.D., Michel Duyne, Ph.D., and Pierre Roubertoux, Ph.D.
Paris, France

- In 4 of 12 prepubertal autistic children (6–10 years old) in our inpatient child psychiatry department, we have observed precocious secondary sexual characteristics (growth of pubic hair, increase of testis volume) that suggest high androgenic activity in infantile autism. In addition, there are four times more male than female autistic patients.

- To test our hypothesis of a hyperandrogeny and autism association, we measured plasma testosterone and adrenal androgen in nine drug-free inpatients with DSM-IV autism and 62 normal subjects of same age, sex, weight (within 2 kg), and stage of puberty.

- Results showed that three of the nine autistic subjects had an abnormally high plasma testosterone concentration (over two standard deviations above the mean for the comparison subjects), with values above that of the highest in the comparison subjects.

Discussion
The US Department of Health and Human Services and the National Institute of Child Health and Development (NICHD) of the National Institutes of Health (NIH) estimate the incidence of precocious puberty in the general population to be approximately one in 10,000 children (US Department of Health and Human Services 1997). The incidence of precocious puberty has been estimated to be higher in children with neurodevelopmental disabilities than in children without neurodevelopmental disabilities. Our retrospective review of this population with neurodevelopmental disabilities suggested that a child with a neurodevelopmental disability was at least 20 times more likely to experience early pubertal changes.
A summary of the interaction between the transsulfuration and androgen pathways in autistic spectrum disorders

**Clinical Effects of Elevated Androgens in Autism Spectrum Disorders & their Family Members?**

- Data were available for 38 women with autism and from an age-matched comparison group of 38 females without autism.
- Three of the women in the autism group had their first period at a very late age (20y, 20y 1mo, 20y 3mo).
- Even excluding these women, women with autism, on average, began their periods at a later age than the women in the control group (13y 4mo vs 12y 7mo respectively).
- These authors reported that, even though the studies were conducted on children with autism who, at the age of 26, has never experienced menarche.
Testosterone levels are positively correlated with a number of autistic traits and inversely correlated with social development and empathy.

A medical questionnaire was completed by n=54 women with ASDs, n=74 mothers of children with ASDs, and n=183 mothers of typically developing children.

Compared to controls, significantly more women with ASDs reported (a) hirsutism, (b) bisexuality or asexuality, (c) irregular menstrual cycle, (d) dysmenorrhea, (e) polycystic ovary syndrome, (f) severe acne, (g) epilepsy, (h) tomboyism, and (i) family history of ovarian, uterine, and prostate cancers, tumors, or growths.

Compared to controls, significantly more mothers of ASD children reported (a) severe acne, (b) breast and uterine cancers, tumors, or growths, and (c) family history of ovarian and uterine cancers, tumors, or growths.

These results suggest current hormone abnormalities in women with ASC and their mothers.

Treatment Overview:

The Protocol

** Children are administered a Lupron (leuprolide acetate) Depot 15 mg / 14 days. Children also are supplemented with daily non-depot Lupron dosing (0.2 mL = 1 mg Lupron).

** Total starting dose = 100 ug / Kilogram bodyweight / day.

** Patients are monitored as successive doses of Lupron Depot are administered for persistent clinical/laboratory signs of increased androgens, and patients are supplemented with daily non-depot dosing, Aldactone, and/or Androcur as necessary.

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Table 2. An evaluation of the effects of treatment on CGI in the study group of children with autism spectrum disorders using the Autism Treatment Evaluation Checklist (ATEC)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Median Improvement Score</th>
<th>Median Sociality Score</th>
<th>Median Capabilities Score</th>
<th>Median Behavior Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10 (6-15)</td>
<td>10 (6-15)</td>
<td>10 (6-15)</td>
<td>10 (6-15)</td>
</tr>
<tr>
<td>End of Study Period</td>
<td>4 (0-8)</td>
<td>6 (0-12)</td>
<td>6 (0-12)</td>
<td>6 (0-12)</td>
</tr>
</tbody>
</table>

*p < 0.05

This non-parametric Mann-Whitney U test analysis was employed to derive the statistical significance.
Furthermore, in our own clinical experience we have observed that leuprolide acetate (LUPRON®) administration to nearly 200 patients diagnosed with ASDs significantly lowered androgen levels and has resulted in very significant overall clinical improvements in socialization, sensory/cognitive awareness, and health/physical/behavior skills, with few non-responders and minimal adverse clinical effects to the therapy.

The following are some specific areas of significant clinical ameliorations in frequent symptoms that occur in patients diagnosed with ASDs observed:

- hyperactivity/impulsivity
- stereotypy
- aggression
- self-injury
- abnormal sexual behaviors
- irritability behaviors
Diazepam = Valium
Fluoxetine = Prozac
Overall Summary of Testosterone Lowering Medications:

1. Anti-Hypertensives (Inderal, Clonidine, Reserpine, Lasix, etc.)
2. Antidepressants (SSRIs: Prozac, Celexa, Lexapro, Paxil, Zoloft, and Luvox; SNRIs: Effexor, Pristiq, and Cymbalta; Tricyclics: Elavil, Sinequan, Tofranil, and Anafranil; and MAOIs: Nardil, etc.)
3. Anticholinergics (Benadryl, Donnatal, Pro-Banthine,Cogentin, etc.)
4. Tranquilizers (Haldol, Thorazine, Zyprexa, Seroquel, etc.)

The Reverse:

Clinical Features of High Androgens in Previously Neurotypical Children
Testosterone administration impairs cognitive empathy in women depending on second-to-fourth digit ratio.

Abstract

During social interactions, we automatically infer thoughts, intentions, and feelings from body cues of others, separate from the role of language. This cognitive empathic ability is one of the most important components of social intelligence and is essential for effective social interactions. Previous research has noted an inverse relationship between cognitive empathy and testosterone levels, and the male sex hormone testosterone is thought to be involved. Testosterone may not only down-regulate cognitive empathy organizationally, by affecting brain development, testicular function, and the brain’s response to stress. Our data suggest that the effect of testosterone is strongly related to the second-to-fourth digit ratio. Our data thus further demonstrate that sex ratio regulation affects cognitive empathy, but also suggest these are representative of the sex ratio in the development of human social development.