Can autism be triggered by acetaminophen activation of the endocannabinoid system?

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BACKGROUND FROM DAN MURPHY:

Acetaminophen is available in more than 200 OTC and prescription drugs. It has more than 50 brand names, the best known is Tylenol in the US. Tylenol, a pain/fever drug, is often given to children; parents rarely give children aspirin because of the increased risk of Reye’s syndrome. Acetaminophen is the primary cause of liver toxicity in the US.

An internet search of the Tylenol WebPage finds this information:

“Jr. TYLENOL® Meltaways® Chewable Tablets comes in an easy-to-use form that kids love—Jr. TYLENOL® Meltaways® Chewable Tablets. Fast relief—in yummy Grape Punch and Bubblegum Burst. Meltaways® are easy to give—no spoon and no water needed. And easy to take.”

“Liver warning: This product contains acetaminophen. Severe liver damage may occur if your child takes more than 5 doses in 24 hours, which is the maximum daily amount.”

Importantly, the liver is the primary producer of the detoxifying antioxidant glutathione. Glutathione depends upon the availability of sulfate.

KEY POINTS FROM THIS STUDY:

1) “Autism is a severe developmental disorder defined by social and communication deficits and ritualistic-repetitive behaviors that appear in early childhood.” The cause of autism is unknown in most cases.

2) “Acetaminophen use in children has been associated with increased autism risk.”

3) “Acetaminophen’s analgesic actions result from activation of the endocannabinoid system, and activation of this system can have neuromodulatory consequences during development.”
4) “In this report we present evidence of a link to autism from acetaminophen use, evidence to show that acetaminophen produces analgesia by activating cannabinoid receptors, and evidence that activation of the cannabinoid receptors may interfere with normal [brain] development to trigger autism.”

5) “Children are often given acetaminophen if they have symptoms such as fever or irritability, and the MMR vaccination can cause these symptoms.”


8) Sulfation is the primary pathway for acetaminophen metabolism in children. Children with autism have a deficit in sulfation. This may lead to increased blood levels of acetaminophen after acetaminophen consumption.

9) Children with autism appear to be poor metabolizers of acetaminophen, leading to higher than normal therapeutic levels. “Children who are poor metabolizers of acetaminophen may be at higher [autism] risk since normal therapeutic doses may lead to higher blood levels in these children.”

10) Acetaminophen produces analgesia by activating cannabinoid receptors in the brain.

11) “The endocannabinoid system plays an important role in the development of the central nervous system and its [inappropriate] activation can induce long-lasting functional alterations.”

12) “Use of cannabis (an exogenous cannabinoid [marijuana]) in the still-maturing brain may produce persistent alterations in brain structure and cognition.”

13) In the CNS, cannabinoid receptors help develop areas in the brain that are dysfunctional in autism:
   • Cerebellum
   • Hippocampus
   • Basal ganglia
   • Neuron differentiation
   • Proper axonal migration
   • Defining synapse positioning
14) Acetaminophen interference of the cannabinoid receptors could trigger autism by interrupting normal brain development.

15) Acetaminophen also dysregulates brain immune system function, leading to autoimmunity against brain and central nervous system proteins. These authors propose that this immune dysregulation in children with autism is due to the influence of acetaminophen during gestation or in early childhood.

16) “The blockage of fever with antipyretics (as acetaminophen) could lead to autism by interfering with normal immunologic development.”

17) Other environmental factors that may trigger autism include:

- Low levels of breastfeeding, decreasing immune protection in infants by decreasing mother to child transfer of IgA.
- Lack of breastfeeding is associated with autism.
- Use of infant formula without docosahexaenoic acid or arachidonic acid supplementation is associated with autism.

COMMENTS FROM DAN MURPHY

We have reviewed other studies that have also noted a link between acetaminophen consumption and autism:

**Article Review 10-12**: Helen V. Ratajczak; Theoretical aspects of autism: Causes—A review; Journal of Immunotoxicology; January 2011; Vol. 8; No. 1; pp. 68–79:

- “Acetaminophen has also been suggested to cause autism.”
- “Children given acetaminophen after the MMR II vaccine were significantly more likely to become autistic than children given ibuprofen.”
- “During pregnancy, mothers of autistic children commonly suffer more bacterial and viral infections and fevers, which could affect the fetus to predispose the child for autism. These mothers often take acetaminophen to treat the infections. Acetaminophen overdose depletes the liver’s supplies of sulfate and glutathione, impairing its ability to detoxify and excrete harmful substances. Therefore, the fetus could be impaired by the mother’s consuming acetaminophen. After birth, if acetaminophen were given to the child, and used repeatedly, the drug could cause depletion of sulfate and glutathione, and the child could regress into autism.”
**Article Review #38-13**: Stephanie Seneff, Robert M. Davidson and Jingjing Liu; Empirical Data Confirm Autism Symptoms Related to Aluminum and Acetaminophen Exposure; Entropy; November 7, 2012; 14; pp. 2227-2253:

- “A strong correlation between autism and the MMR (Measles, Mumps, Rubella) vaccine is also observed, which may be partially explained via an increased sensitivity to acetaminophen given to control fever.”

- MMR is significantly more likely to be associated with autism. “An interesting theory relating the MMR vaccine to autism involves a proposed toxic reaction to the acetaminophen (paracetamol) administered to control fever following vaccination.”

- “If the MMR vaccine is administered simultaneously with DTaP, an aluminum-containing vaccine (as is often the case), then the acetaminophen would likely interfere with the child’s ability to dispose of the aluminum.”

- “Hep-B is administered usually within 24 hours of birth, and most definitely in the first two months of life, and HiB Titer is administered three or four times before the age of 15 months. These two vaccinations would thus cause an accumulation of mercury and aluminum along with a depletion of the bioavailability of sulfate prior to the MMR vaccine in the vulnerable child, leaving them more susceptible to an infection arising from the live virus administered in MMR, and a subsequent dose of Tylenol (acetaminophen) to curb fever.”

- Acetaminophen would also deplete sulfate needed to detoxify aluminum in any concurrent aluminum-containing vaccine such as DTaP.

- “While the autism community has focused on the mercury in thimerosal as the main culprit in vaccines, our studies with the VAERS database have identified aluminum and acetaminophen as being likely even more damaging than mercury.” “Because of the sulfur deficiencies, aluminum, mercury and acetaminophen likely accumulate in the autistic brain, leading to further damage.”

- We hypothesize that the fever associated with MMR results in the administration of acetaminophen, which, in conjunction with the intense immune response to live viruses, becomes toxic to the vulnerable child.”

- We “observed a strong correlation between the MMR vaccine and autism, which we suggest could be explained by the effects of acetaminophen.”