

Nutritional Challenges in Children with Autism

Cade Nylund, MD, MS
Major, United States Air Force, Medical Corps
Assistant Professor of Pediatrics
Uniformed Services University of the Health Sciences



Disclosure

- I have no financial relationships to disclose or conflicts of interest to resolve.
- The views expressed here are my own and do not reflect the official policy of the United States Air Force, the Department of Defense, or the U.S. Government.



Objectives

- Identify the specific nutritional risks of children with autism
- Understand unique features of autism which place children at risk of malnutrition
- Review recent developments on specific nutritional supplements or diets in children with autism



What is Autism?

Autism Spectrum Disorder (ASD)

- Lifelong Disorder
- Spectrum of Neurodevelopmental Conditions
- Deficits in Communication and Social Interactions
- Repetitive Behaviors
- Restricted interests and activities
- CDC Reports 1/68 Children affected

Baio J. *MMWR* March 2014
American Psychiatric Association. DSM 5th ed. Arlington, VA: American Psychiatric Association; 2013



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Case 1

- 5 year old boy diagnosed with ASD at age 3
- Non-verbal and significant cognitive delay
- Has severe selective feeding disorder
 - Brand specific macaroni and cheese
 - Brand, flavor, and color specific fish crackers
 - Will eat no other foods
 - Mother has tried “everything” to try to broaden his nutritional intake



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Case 1

- Height 109 cm Weight 15.2 kg
- BMI 12.8 kg/m² Z Score -3.17
- 25-OH Vitamin D 16.2 ng/ml
- CBC and Iron panel normal
- Treatment Plan
 - Treated Vitamin D deficiency
 - Made referral to intensive inpatient feeding program
 - Feeding team sent the patient back to have an EGD prior to enrollment in their feeding program

Case 1

- Esophagogastroduodenoscopy Performed



- Identified Eosinophilic Esophagitis (EoE)



Case 1

- Topical steroid treatment for EoE
- Repeat EGD proved adequate treatment
- Enrolled in inpatient intensive behavioral feeding program
- Broadened diversity of this diet
- 6 month follow up BMI Z-score -1.8



Case 2

- 17 year old male with ASD
- Developmental delay, but verbal
- On atypical antipsychotic for behavioral outbursts
- BMI 36 kg/m²
- Dietary/Activity History: 2-3 gallons of sweet tea per day, and No activity
- Increased aminotransferases suggestive of NAFLD or NASH



Case 2

- Artificial Sweetened Beverages replaced his sweet tea
- Encouraged to walk his Yorkshire Terrier twice a day
- 3 months later he had lost 12 kg
- Aminotransferases levels improved



Why Nutritional Challenges?

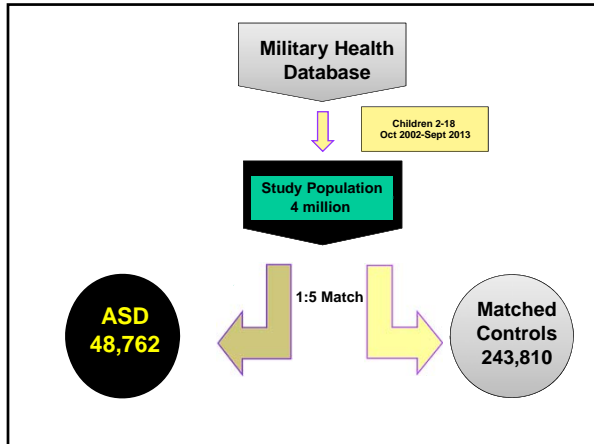
- Undernutrition
 - Frequent feeding disorders
 - Self-initiated selective eating
 - Parent-initiated selective diets
- Overnutrition/hyperalimantation
 - Decreased physical activity
 - Rewarded with preferred foods
 - Selective eating of high calorie/ low nutrient dense (aka junk) foods
 - Medications which may stimulate appetite

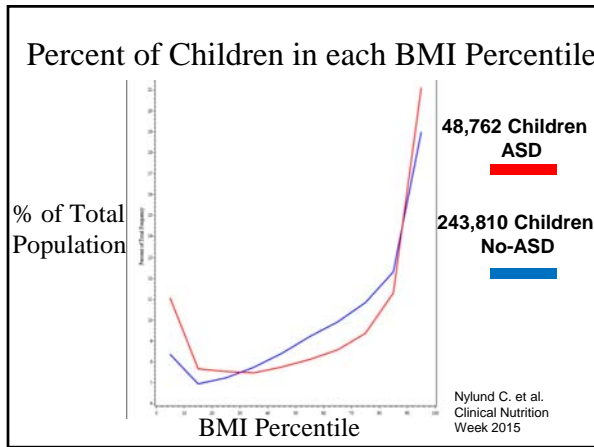


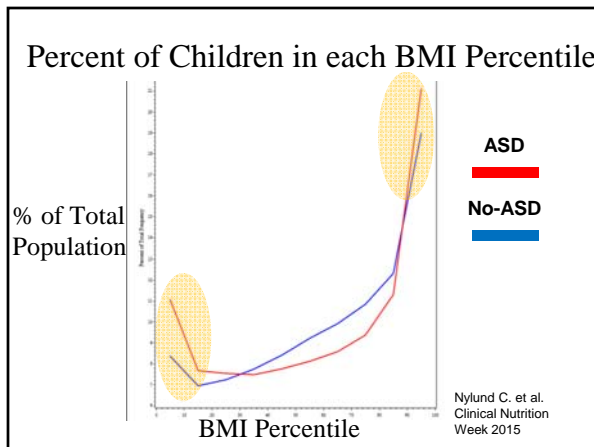
Military Health Care Data on Children with ASD

- Have large population of children
 - Around 1 million at any time
- Demographically, geographically, and socioeconomically diverse background
- Largest single cohort of children with ASD

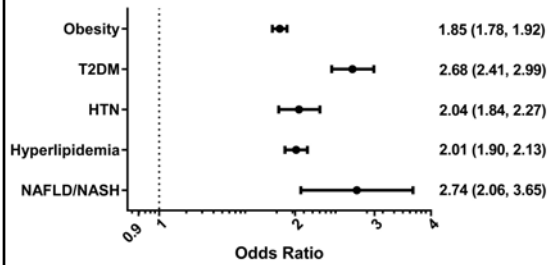








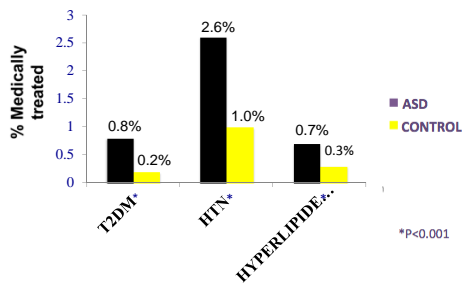
Association of a Diagnosis of ASD with Obesity and Metabolic Comorbidities



T2DM=Type 2 Diabetes Mellitus, HTN = Hypertension

Shedlock K Pediatric Academic Society Annual Meeting, San Diego, CA, May 2015.

Percentage of Pediatric Patients with ASD and Controls Requiring Medication for Metabolic Complications of Obesity



T2DM=Type 2 Diabetes Mellitus, HTN = Hypertension

Shedlock K Pediatric Academic Society Annual Meeting, San Diego, CA, May 2015.

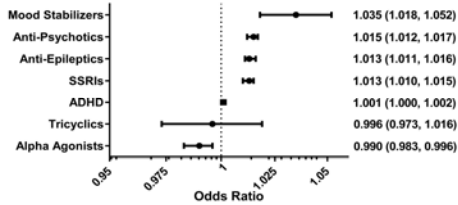
ASD and Obesity in Adulthood

- 92 Adult subjects with ASD
- 45 % were obese or overweight
- 15 % Hyperlipidemia
- 11 % Hypertension
- 10% Diabetes

Jones KB. *Autism* 2015 July. Epub ahead of print



Association of Psychotropic Medications with Obesity for Children with ASD



Shedlock K. Pediatric Academic Society Annual Meeting, San Diego, CA, May 2015.



ASD, Obesity, and Age

- Younger children with ASD take in significantly less calories than controls
- The risk of obesity is highest in the teenagers (12-20 years old)

Broder-Fingert S. Acad Pediatr. 2014 Jul-Aug 14:408-14
Hyman SL. Pediatrics 2012 Nov 130:S145-153



ASD, Obesity and Micronutrient Deficiency

- Despite excess in calorie intake, children with ASD and obesity consume insufficient
 - Iron
 - Calcium
- More likely to be vitamin D deficient

Shmaya Y. Research in Developmental Disabilities. 2015 Mar 38, pg 1-6



Summary Obesity and ASD

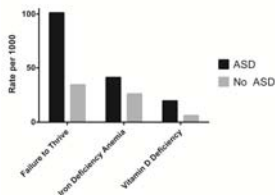
- Nearly twice as likely to be obese
- Metabolic Complications of Obesity
 - Hypertension
 - Type 2 Diabetes Mellitus
 - Hyperlipidemia
 - NAFLD/NASH
 - More likely to be prescribed medication, suggests less likely to respond to nutritional intervention and exercise alone
- Psychotropic Medication are associated with obesity in children with ASD
- Children with ASD often have micronutrient deficiency despite excess in calories





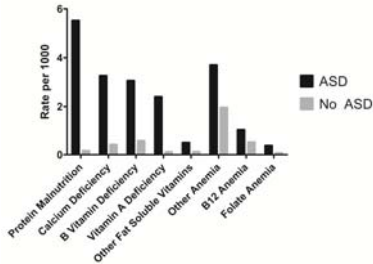
Malnutrition

- Micronutrient deficiencies common
- 16 % diagnosed with malnutrition
- 10 % with diagnosis of failure to thrive



Nylund C. et al. Clinical Nutrition Week 2015

Specific Micronutrients



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Nylund C. et al. Clinical Nutrition Week 2015

Feeding Disorders in ASD, and Malnutrition

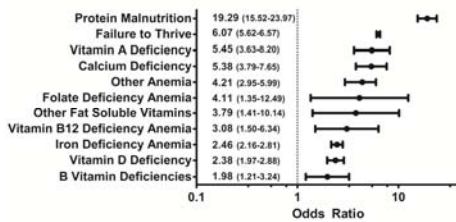
- 6.5 % of children with ASD are diagnosed with a feeding disorder
- 0.8 % of controls
- Odds Ratio 8.0 (7.5-8.5)
- Feeding disorder is a red flag for malnutrition



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Among those with ASD Risk of Malnutrition if Patient Diagnosed with Feeding Disorder



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Eosinophilic Esophagitis (EoE)

- Feeding disorders are the most highly associated comorbid diagnosis in pediatric onset EoE
- Feeding disorders are often assumed to be behavioral in children with ASD
- Children with ASD are at an increased risk of EoE
 - Odds Ratio 2.94 (2.45-3.53)
- ASD w/ Feeding disorder Odd Ratio of EoE
 - 24.2 (8.1-72)
- No ASD w/ Feeding disorder Odds Ratio of EoE
 - 21.8 (5.5-87.9)



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Heifert et al. NASPGHAN 2015

Feeding Disorders and ASD

- Feeding disorders should not be assumed to be behavioral
- EGD should be performed

- EoE is a treatable disease which potentially lead to improved caloric intake



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Picky Eaters

- Pathologic feeding disorder
 - Evidence of malnutrition
 - <10-20 foods
- Picky Eater
 - No evidence of malnutrition
 - Eats a variety of foods maybe doesn't like specific textures, colors, etc.

- Pathologic feeding disorder
 - Rule out EoE or other organic cause, aspiration, swallowing problem etc.
 - Refer to a specialty feeding therapy program

- Picky
 - Recommend “Just Take a Bite” as first step for parents
 - Referral to pediatric speech therapist





Special Diets and ASD

- Inconclusive evidence that Gluten-Free, Casein-Free (GFCF) diet or any other diet improves the primary symptoms of autism
- Children may require special diets for other comorbid conditions



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Millward C et al. Cochrane
Database Syst Rev 2008

ASD and Special Diets

- Specific diets may be required to treat specific disorders in those with ASD
 - Eosinophilic Esophagitis
 - Celiac disease
 - Food Allergies

Mulloy A et. al. *Research in Autism and Developmental Disorders* 2010



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Existing Evidence for GFCF diet

- Randomized Study of 20 children in Norway
- All children had abnormal urinary peptides
- 1 year GFCF diet
- Follow up blinded assessments
- Significant improvement in multiple developmental domains for those on the diet

Knivsberg AM. et al. *Nutr Neurosci* 2002 Sep;5(4):251-61

GFCF Diet Study Issues

- Small study of 10 kids with ASD
- All had abnormal peptides excreted in the urine

- Children with ASD on GFCF diet had 19% reduced cortical bone thickness

Hediger M et al. *J Autism Dev Disorder*. 2008;38:848-856

Nutritional Supplements & ASD

- Omega-3 FA-- evidence inconclusive
- Methylcobalamin and L-Methylfolate evidence still inconclusive and further studies needed
 - May be related to an association in the MTHFR gene in only some children

James s. et al. *Cochrane Database Syst Rev* 2011

Frye RE et al. *Autism Res Treat.* Oct 2013



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Clinical Study

Effectiveness of Methylcobalamin and Folinic Acid Treatment on Adaptive Behavior in Children with Autistic Disorder Is Related to Glutathione Redox Status

Richard E. Frye,¹ Stepan Melnyk,¹ George Fuchs,¹ Tyra Reid,¹ Stefanie Jernigan,¹ Olesksandra Pavliv,¹ Amanda Habanks,¹ David W. Gaylor,² Laura Wallers,¹ and S. Jill James¹

¹Department of Pediatrics, Arkansas Children's Hospital Research Institute, University of Arkansas for Medical Sciences, Little Rock, AR 72202, USA

²Department of Biostatistics, Arkansas Children's Hospital Research Institute, University of Arkansas for Medical Sciences, Little Rock, AR 72202, USA

Correspondence should be addressed to Richard E. Frye, rcfrye@uams.edu

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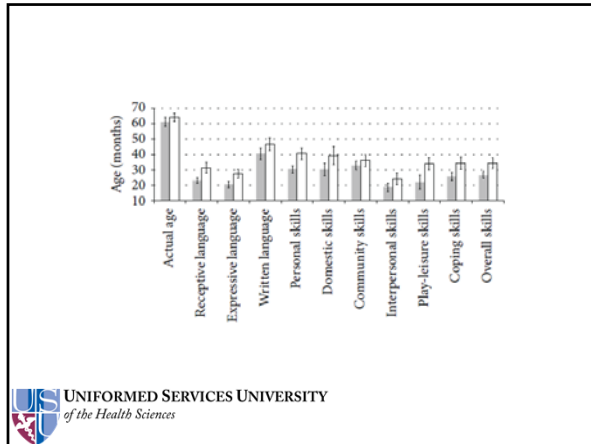
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Treatments targeting metabolic abnormalities in children with autism are limited. Previously we reported that a nutritional treatment significantly improved glutathione metabolism in children with autistic disorder. In this study we evaluated changes in adaptive behaviors in this cohort and determined whether such changes are related to changes in glutathione metabolism. Thirty-seven children diagnosed with autistic disorder and abnormal glutathione and methylation metabolism were treated with twice weekly 75 µg/kg methylcobalamin and twice daily 400 µg folinic acid for 3 months in an open-label fashion. The Vineland Adaptive Behavior Scale (VABS) and glutathione redox metabolites were measured at baseline and at the end of the treatment period. Over the treatment period, all VABS subscales significantly improved with an average effect size of 0.59, and an average improvement in skills of 27 months. A greater improvement in glutathione redox status was associated with a greater improvement in expressive communication, personal and domestic daily living skills, and interpersonal, play-leisure, and coping social skills. Age, gender, and history of regression did not influence treatment response. The significant behavioral improvements observed and the relationship between these improvements to glutathione redox status suggest that nutritional interventions targeting redox metabolism may benefit some children with autism.

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Methylenetetrahydrofolate Reductase (MTHFR)

- 1672 with ASD vs. 6760 without ASD
- Several specific C677T polymorphisms associated with ASD
 - Odds ratios range for various polymorphisms was 1.42-1.86

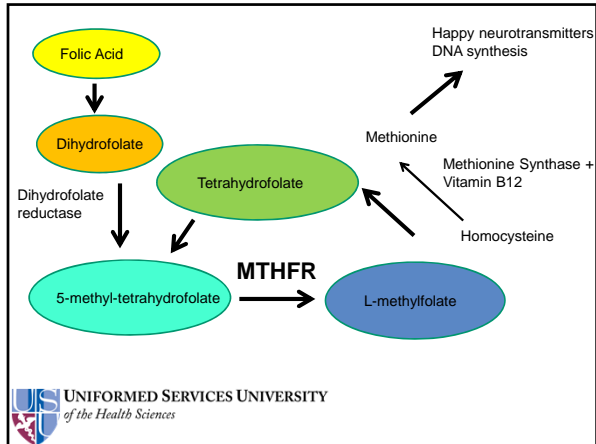
Pu D. et al. *Autism Research*. Oct 2013; 6(5):384-92

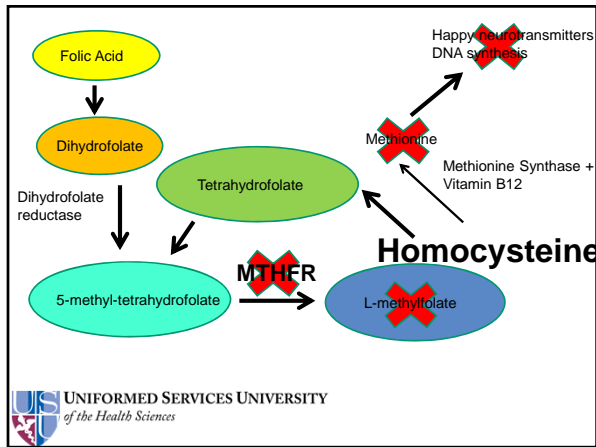
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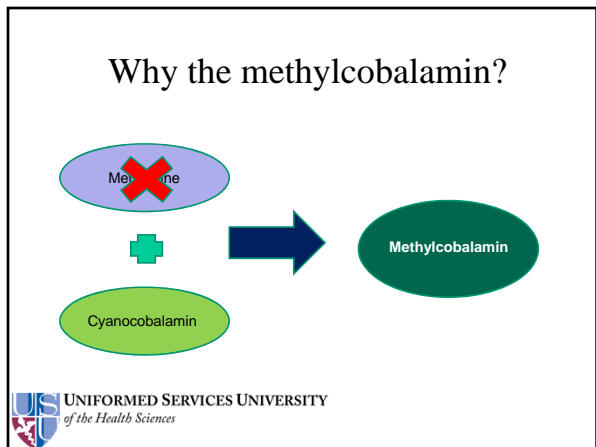
Folic Acid Review

- Folate required for DNA/RNA synthesis and cell repair
- Critical during times of cell growth
 - One of the signs of deficiency is anemia
- Involved in neurotransmitter synthesis
 - Dopamine
 - Serotonin
 - Norepinephrine

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L-Methylfolate and Methylcobalamin Approach

- There is evidence that MTHFR enzyme deficiency is linked to autism **in some children**
- Supplementation **may** be helpful only in children who have a MTHFR mutation
- Genetic testing is available
- “Poor man’s test” = homocysteine level
- All children with ASD on a multivitamin

Children with ASD Nutritional Call to Action

- Early health nutritional maintenance/supervision as routine care for all children with ASD
- Early parent education on nutritional risks
- Identify pathological cause of symptoms (EoE)
- Parent training and referral to speech/feeding therapy for selective feeding or feeding disorders
- Multidisciplinary approach
 - RD, Speech Therapy, Occupational Therapy, Psychiatry, GI, Developmental Peds, PCM





Questions?