United States



A case-control study of dietary salt intake and risk of pediatric multiple sclerosis (MS)

J McDonald, J Graves, A Waldman, T Lotze, T Schreiner, A Belman, B Greenberg, B Weinstock-Guttman, G Aaen, J-M Tillema, J Hart, J Ness, J Rubin, L Krupp, M Gorman, L Benson, M Rodriguez, T Chitnis, S Mar, LF Barcellos, J Rose, S Roalstad, T Simmons, TC Casper, E Waubant

Disclosures

Authors have no disclosures relevant to this work.

Background

Limited research on dietary salt and MS

- Association between salt intake and disease activity
- Link between high salt and disease onset and progression in animal model
- Salt proposed to enhance pro-inflammatory pathways
- Pediatric-onset MS offers opportunity to study nutritional risk factors close to disease onset

Objective

To determine whether dietary salt intake is associated with pediatric-onset MS

Methods

Multicenter, case-control design

- 14 US pediatric MS centers (Nov. 2011-Jun. 2014)
- Collaborative investigation on environmental and genetic factors in children with MS (R01NS071463, PI Waubant)
- Each center collected:
 - Demographics
 - Environmental exposures
 - Medical history

Methods, cont.

Study participants

Cases

- Children with CIS with at least 2 silent T2 lesions or RRMS based on McDonald criteria
- Onset < 18 years of age, < 4 years duration

Controls

- Recruited at same participating centers
- < 20 years of age</p>
- Exclusion criteria:
 - No history of autoimmune disorders (except eczema and asthma)
 - No history of immunosuppressive therapy
 - Parental MS

Methods, cont.

Blocks Kids Food Screener

- Children 2-17 YO (English/Spanish), 10-12 minutes to complete
- Self-report, validated dietary screener
- Subjects select frequency and portion of food consumed in the previous week
- 41 questions including:
 - Fruits/fruit juices, vegetables
 - Processed foods, including French fries
 - Meat, poultry, fish, whole grains, dairy, legumes

Statistical Analyses

- Sodium intake was compared between cases and controls
 - Continuous variable
 - Categorical variable based on excess sodium
 - Terciles
- Logistic regression models adjusted for:
 - Age
 - Gender
 - Body mass index (BMI)
 - Ethnicity
 - Socioeconomic status (SES)

Results, baseline characteristics

	Cases N=174	Controls N=337	All N=511	P-value
Age (mean +/- SD)	15.2 (3.4)	13.9 (3.7)	14.4 (3.6)	<.01
BMI (kg/m²)	25.1 (6.5)	22.0 (5.9)	23.0 (6.3)	<.01
Energy (kcal/day)	1322 (602)	1315 (631)	1371 (620)	0.85
Total fat (g/day)	53.8 (28.4)	53.6 (28.5)	53.6 (28.4)	0.99
Gender				<.01
Female	110 (63%)	164 (49%)	274 (54%)	
Race				0.09
White	101 (58%)	230 (68%)	331 (65%)	
Ethnicity				<.01
Hispanic or Latino	51 (29%)	59 (18%)	110 (22%)	
Mother's highest degree				<.01
None	22 (13%)	17 (5%)	39 (8%)	
High school, associates	96 (55%)	138 (41%)	234 (46%)	
Bachelor's, graduate	50 (30%	143 (42%)	193 (38%)	
Other	0 (0%)	12 (4%)	12 (2%)	

Results, dietary sodium intake

	Gender	Cases	Controls	All	P-value
Sodium (mg/day <u>+</u> SD)	All	2025 (1096)	2007 (1094)	2013 (1094)	0.98
	Male	2496 (1242)	2327 (1290)	2373 (1277)	0.27
	Female	1751 (899)	1668 (697)	1701 (784)	0.77

Results, dietary sodium intake

	Gender	Cases	Controls	All	P-value
Excess sodium (%)	All	64	68	67	0.34
	Male	81	77	78	0.53
	Female	54	58	56	0.48

- No difference in proportion of cases vs. controls who consumed excess sodium
- Excess sodium defined by adequate intake:
 - 1000 mg/d (1-3 YO)
 - 1200 mg/d (4-8 YO)
 - 1500 mg/d (9-19 YO)

Institute of Medicine, Dietary Reference Intakes

Results, dietary sodium intake

Sodium terciles	Gender	Cases	Controls	All
1 st	All	36%	32%	33%
	Male	22%	23%	23%
	Female	44%	41%	42%
2 nd	All	31%	35%	33%
	Male	27%	29%	28%
	Female	34%	41%	38%
3 rd	All	33%	33%	33%
	Male	52%	48%	49%
	Female	23%	18%	20%

No difference in proportion of cases versus controls in each tercile (p=0.63)

No relationship between tercile and case-control status for males (p=0.88) or females (p=0.40)

Results, multivariable analyses

	OR	95% CI	P-value
Sodium (100 mg/day)	1.00	(0.98, 1.02)	0.79
Excess sodium	1.06	(0.68, 1.67)	0.79
Log (sodium)	1.11	(0.71, 1.73)	0.64
Sodium terciles			
2 nd versus 1 st	0.97	(0.58, 1.62)	0.90
3 rd versus 1 st	1.15	(0.67, 1.98)	0.60

Adjusted for age, gender, BMI, ethnicity, SES

Discussion

Strengths

- Case-control design with large catchment area, diverse patient population
- Foods high in sodium included in dietary screener
- Multivariable analyses adjusted for factors associated with both MS risk and diet

Limitations

- Self-report assessment can be limited by subject recall and foods listed on screener
- Dietary patterns may have changed since diagnosis

Conclusions

- No difference in dietary salt intake was found between cases and controls in unadjusted analyses and multivariable regression models
- If confirmed, dietary salt intake may not play a large role in pediatric MS susceptibility

Future Direction

- Salt associated with MS risk in sub-group with specific genotypes or unidentified risk factors?
- Salt associated with relapse rate or disease activity?

Acknowledgements

Thank you to the patients and their families for taking the time to be part of this research

Supported by:

- NIH: R01NS071463-03, PI E. Waubant
- The National MS Society: Grant, HC0165, PI T.C. Casper

Participating Centers & Collaborators:

- UCSF: J. Hart, J. Graves, S. Lulu, M. Lee
- UC Berkeley: LF Barcellos
- Stony Brook: L. Krupp, A. Belman, M. Milazzo
- Mass General: T. Chitnis
- Children's Boston: M. Gorman, L. Benson
- University of Buffalo: B. Weinstock-Guttman
- University of Alabama, Birmingham: J. Ness
- Mayo: M. Rodriguez, M. Patterson, J-M. Tillema
- Loma Linda: G. Aaen
- Children's Houston: T. Lotze
- Children's Hospital Philadelphia: A. Waldman
- Ann & Robert H. Lurie Children's Hospital: J. Rubin
- UT Southwestern: B. Greenberg
- Children's Denver: T. Schreiner
- Washington University: S. Mar
- University of Utah: C. Casper, J. Rose, S. Roalstad