ASSOCIATIONS OF CHILDHOOD FACTORS WITH MS, NMO, AND TM

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DISCLCOSURES

- The presenters have no disclosures to report

BACKGROUND

- Environmental and lifestyle exposures such as smoking, infectious mononucleosis, HLA-DR15, and EBV infection are associated with **MS** risk [1].
- These same factors are **not** associated with risk for **NMO** or **TM** [1].
- Early-life exposures of breastfeeding and daycare attendance have been shown to have protective effects for adult-onset **MS**, pediatric-onset **MS**, and pediatric **NMO** [2].
- Passive smoke exposure during childhood has been shown to increase risk of pediatric **MS** [3].

RATIONALE

- There is evidence that early-life **environmental** and **lifestyle** exposures are associated with risk for adult-onset **MS**, pediatric **MS**, and pediatric **NMO**.

- Therefore, we *hypothesize* that other early-life exposures may also contribute to variation in the risk for **adult-onset** **MS**, **NMO** and **TM**.

OBJECTIVE

- To determine if the following early-life exposures are associated with risk of **MS**, **NMO** and **TM:**
  - **mother's age at birth**
  - **father's age at birth**
  - **breastfeeding status**
  - **breastfeeding duration**
  - **mother's smoking status during pregnancy**
  - **household smoking during childhood**

Study population

- This study includes 2,255 participants from the Accelerated Cure Project.
- The population includes 1,264 **MS**, 330 **NMO**, and 166 **TM** patients as well as 495 healthy controls.
- The onset age variable was used to filter for cases of **MS**, **NMO**, and **TM** that were adult onset (onset age ≥ 18 years, n = 2,220).

Study Design

- Six childhood factors were identified: **mother's age at birth**, **father's age at birth**, **breastfeeding status**, **breastfeeding duration**, **mother's smoking status during pregnancy**, and **household smoking during childhood**.
- Six logistic regression models were run with **each disease as the dependent variable**. Each model included age, sex, race, and **one of the childhood factors of interest** **as the predictor of interest**. A two-sided alpha of 5% was considered statistically significant.

RESULTS

Study population characteristics

- For each set of logistic regression models, one of the case groups was compared to the control group.

Phenotype		MS	NMO	TM	Control	p
n		1,264	311	150	495	
Birth year mean (SD)		1962 (11.2)	1964 (12.4)	1958 (12.7)	1962 (16.5)	.02
Male		23.3%	15.1%	32.7%	32.1%	<.001
Race (%)	White	89.2%	74.0%	92.7%	68.5%	
	Black	8.0%	17.7%	4.7%	6.9%	<.001
	Other	2.8%	8.4%	2.7%	24.6%	
Breastfeeding status (%)	No	55.4%	44.1%	51.3%	31.9%	
	Yes	30.7%	41.8%	36.0%	31.9%	<.001
	Missing	13.9%	14.1%	12.7%	36.2%	
Mother's smoking status during pregnancy (%)	No	59.8%	67.2%	63.3%	47.1%	
	Yes	24.8%	17.7%	20.7%	18.8%	<.001
	Missing	15.4%	15.1%	16.0%	34.1%	
Household smoking during childhood (%)	No	32.6%	38.9%	36.0%	29.7%	
	Yes	62.0%	58.2%	58.7%	43.0%	<.001
	Missing	5.4%	2.9%	5.3%	27.3%	
Breastfeeding duration median [IQR]		0.0 [0.0, 0.0]	0.0 [0.0, 2.0]	0.0 [0.0, 0.5]	0.0 [0.0, 3.0]	<.001
Mother's age at birth mean (SD)		27.6 (5.7)	27.2 (6.2)	26.7 (5.6)	28.0 (6.1)	.096
Father's age at birth mean (SD)		30.5 (6.6)	30.5 (6.8)	29.1 (6.2)	30.7 (7.1)	.117

MS Results

- There is a protective effect of **breastfeeding** on MS risk ($p<0.001$). Thus, the odds of MS for participants who were *not* breastfed is 1.7 times higher than for those who were breastfed.
- There was also a protective effect on **MS** risk associated with **duration of breastfeeding**. For each additional month of breastfeeding, the **MS** risk was reduced by a factor of 0.95 ($p<0.001$).
- **Household smoking during childhood** is associated with 1.4 times increased odds of **MS** ($p=0.01$)

Early-life exposure	Odds Ratio	95% CI	p
Mother's age at birth	0.99	0.97, 1.01	0.28
Father's age at birth	1.00	0.98, 1.01	0.71
Mother's smoking status during pregnancy	1.04	0.79, 1.38	0.77
Household smoking during childhood	1.40	1.08, 1.79	**0.010**
Breastfed	0.59	0.45, 0.76	**<0.001**
Breastfeeding duration	0.95	0.92, 0.98	**<0.001**

* *adjusted for sex, birth year, and race*

NMO Results

- We did not observe any association between **NMO** and our variables of interest.
- The association between **NMO** and **breastfeeding** that was observed in pediatric-onset cases was **not** seen in this adult-onset population.

Early-life exposure	Odds Ratio	95% CI	p
Mother's age at birth	0.98	0.95, 1.01	0.15
Father's age at birth	1.00	0.97, 1.02	0.69
Mother's smoking status during pregnancy	0.82	0.55, 1.23	0.35
Household smoking during childhood	1.32	0.94, 1.87	0.11
Breastfed	0.98	0.70, 1.39	0.92
Breastfeeding duration	0.99	0.96, 1.02	0.66

* *adjusted for sex, birth year, and race*

TM Results

- There was a protective effect on TM associated with **mother's age at birth of participant**. For each additional year of mother's age, TM risk was reduced by a factor of 0.966 ($p<0.05$).
- Similarly, there was a protective effect on TM associated with **father's age at birth of participant**. For each additional year of father's age, TM risk was reduced by a factor of 0.97 ($p<0.05$).

Early-life exposure	Odds Ratio	95% CI	p
Mother's age at birth	0.966	0.932, 0.999	**0.047**
Father's age at birth	0.967	0.937, 0.997	**0.032**
Mother's smoking status during pregnancy	0.77	0.47, 1.24	0.29
Household smoking during childhood	1.03	0.68, 1.57	0.89
Breastfed	0.74	0.49, 1.13	0.17
Breastfeeding duration	0.95	0.89, 1.00	0.086

* *adjusted for sex, birth year, and race*

CONCLUSIONS

- We replicated the protective effect for breastfeeding in infancy on **MS** risk (OR=0.58, $p=2x10^{-5}$), which decreased by 5% ($p=4x10^{-4}$) per month increase in breastfeeding. There were no relationships between breastfeeding and **NMO** or **TM** risk.

- For each year decrease in maternal and paternal age, **TM** risk increased by 3.8% (p=0.03) and 3.6% (p=0.02) – it is possible this may be due to sampling variability and warrants replication. Parental age was not associated with **NMO** or **MS** risk.

- Maternal smoking during pregnancy was not associated with MS, **NMO**, or **TM** risk.

- Passive smoke exposure in childhood conferred increased risk for **MS** (OR=1.4, p=0.01) with a trending relationship in **NMO** (OR=1.32, p=0.11), but not **TM**.

Summary:

1. We conducted the first study to investigate childhood exposures on adult-onset **NMO** and **TM** risk.
2. We replicated prior **MS** findings, but did not observe strong evidence for relationships with **NMO** or **TM** risk.
3. More research is necessary to explore the relationship between genetic predisposition and early-life exposures.