

NPMSC Newsletter

The Network of Pediatric Multiple Sclerosis Centers (NPMSC)

Welcome to the second issue of the NPMSC Newsletter! The year has flown by and we're excited to bring you this issue. A lot of research progress has been made in the last year. Inside, we hope you enjoy learning about how children with MS and their families continue to contribute to research efforts in a major way and our latest findings from network research studies.

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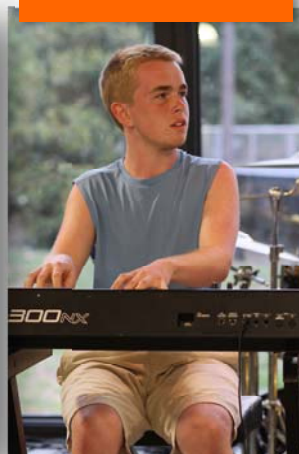
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John and David



Alyssa, Carolyn and Erilyn

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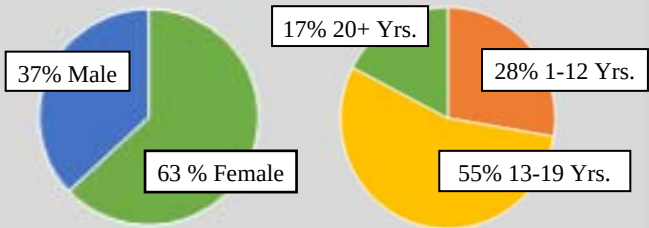
The NPMSC is a United States based network with international collaborations. We are comprised of adult and child neurologists, scientists and other research professionals whose unifying mission is to uncover the mechanisms underlying multiple sclerosis through the study of pediatric-onset demyelinating diseases and to improve the lives of children and families living with these diseases.

Research is important to discovering the best treatment approaches for kids with MS. As kids develop into adults, there are special windows in development that may hold the keys to understanding how MS starts and how to prevent MS. The NPMSC is supported by the National MS Society.

Medical Heroes

We now have over 2,200 children and adolescents in the United States participating in our research studies! Thank you for giving the gift of clinical research participation. You are truly our most important partners in studying pediatric-onset demyelinating diseases—we couldn't do it without you and the support of your family, friends, caregivers and community!

Teens and young adults make up a large percentage of our research partners and are at a point in their life when they will soon be managing their health more independently. Good relationships with healthcare providers are essential to continuing the good management of demyelinating diseases across the lifespan.



Study participants' gender and age in the Pediatric MS and other Demyelinating Diseases study as of November 2018.

Dr. Weinstock-Guttman, Mara and Brett



NPMSC Spotlight

University of Alabama at Birmingham's Center for Pediatric Onset Demyelinating Diseases (CPODD) at Children's of Alabama Birmingham

CPODD CORE CLINICAL TEAM



Dr. Harris, Dr. Ness, and Sarah Dowdy



Dr. Ness and Dorothy at the Decades Dance Party

The CPODD at Children's of Alabama has been holding an annual family retreat for 10 years now. The retreat is for children, their parents and siblings to learn about pediatric-onset demyelinating diseases while building supportive lifelong friendships. Activities such as boating, swimming, arts, crafts and dancing help families bond and relax. It's a welcome change from day to day living with a chronic condition.

The CPODD clinical research team pictured on the far left cares for one of the highest volume of patients in the NPMSC clinical centers and is one of the six founding centers of the network. All three team members have been with the network since the beginning and have provided exceptional service to the children and families they care for—not to mention being fun to work with!

NEW: Diet & Relapses in Pediatric MS Research Study

The purpose of this study is to better understand if diet and metabolism are connected with MS relapses and disease progression in patients with pediatric-onset MS. The National MS Society funds this research study.

During the 3-year study, up to 500 patients age 7-25 with pediatric-onset MS or clinically isolated syndrome (CIS) will take part at 13 pediatric MS centers across the United States.

Study participants will give a one-time blood sample at enrollment and answer questions about food eaten, vitamins taken, and physical activity at three time points (enrollment, 6-months, 12-months) during the study. Participants at four pediatric MS centers may also give an optional one-time stool sample and additional blood sample. In return for time and effort while taking part in this study, participants will receive \$25-\$100 based on completion of research procedures.

If you or someone you know is interested in participating in this research study, please contact Janace Hart (janace.hart@ucsf.edu) for more information and to locate an enrolling pediatric MS center near you. Together, we will overcome this disease!



*Dr. Emmanuelle Waubant,
Study Lead PI at UCSF*



*Janace Hart,
Research Manager at UCSF*

STARTING SOON: Patient & Family Views on Pediatric Multiple Sclerosis

This study consists of a survey asking patients and families about their perspectives on pediatric MS research priorities and methods. The survey was developed by first conducting focus group discussions with patient and family representatives at three NPMSC centers. Important themes in the focus group discussions were turned into survey questions so that more patients and families can contribute. We believe that people living with the disease will provide unique insight into what research is important to them and what barriers exist for them to participate in research. This knowledge will be used to better guide research priorities and design.

ONGOING: Cognition and Neurodevelopmental Influence (CANDI)

We would like to thank everyone who has participated in the Cognition and Neurodevelopmental Influence (CANDI) study so far! This includes children living with MS, adults living with MS, and children without MS. To date, 171 participants have been enrolled in the CANDI study! We will soon be approaching a very critical and exciting milestone in the study. Beginning in March of 2019, study participants will start returning to clinic for their 24-month follow up study visit. During this time, all participants will be re-evaluated using the same measures with which they were tested two years prior. These assessments include cognitive, academic, psychosocial and behavioral measures. The findings from this trial will provide a significant look into cognition of those living with multiple sclerosis over time, and if/how cognition differs between children with MS and adults with MS and also how it differs between children-with MS and children without MS.

ENDING: Environmental and Genetic Risk Factors for Pediatric MS

Enrollment for this study concluded in March, 2018 with a total of 537 pediatric MS participants and 739 pediatric non-MS/control participants! Several risk factors continue to be analyzed and some interesting findings so far are listed below with reference to the published papers (see page 5). A HUGE Thank You to everyone that helped make this study a success!

Environmental and health-related factors that may influence disease activity

Factor	Risk	Comments
Dietary Saturated Fat ¹⁰	Increased disease activity (relapses)	Saturated fat increases inflammation in the body. Limiting the intake of saturated fats (fats that are solid at room temperature like animal fat) can help limit inflammation. Unsaturated fats (liquid at room temperature like olive oil) are still a necessary part of any diet in moderate amounts.
Vegetable Consumption ¹⁰	Decreased disease activity (relapses)	Vegetable intake decreases inflammation in the body and so increasing vegetable intake is a good step to take to help control disease activity.
Salt Intake ^{18, 20}	No change in disease activity	Salt intake did not change disease activity.

Pregnancy Exposures

Manuscript Summary

This study aimed to determine if prenatal, pregnancy or postpartum-related environmental factors are associated with MS risk in children. The parents of 265 children with MS and 412 children without MS at 16 clinics in the United States completed a comprehensive environmental questionnaire and the two groups were compared. Differences in the frequency of pregnancy-related factors, including mode of delivery, illness during pregnancy, tobacco smoke exposure, vitamin D use and breastfeeding were studied. This study suggests that maternal illness and perinatal exposure to pesticides may contribute to MS risk and that C-section delivery is not a risk.

What's Known on This Subject: Previous studies of autoimmune diseases have found breastfeeding to be protective and C-section delivery to be a risk, this study does not confirm these findings.

What This Study Adds: This study suggests that maternal illness and perinatal exposure to pesticides may contribute to risk of pediatric MS.

Full Manuscript: Graves, J. et al, Maternal and perinatal exposures are associated with risk for pediatric-onset MS; *Pediatrics*, Volume 139, Issue 4, April 2017.

Air Quality

Manuscript Summary

Air quality has been identified as a risk factor of interest for pediatric MS, and this study took a closer look at the association between specific air pollutants as well as specific areas of toxic release. The residence of 290 children with MS and 442 children without MS were compared for pollutant exposure and closeness to Toxic Release Inventory (TRI) sites. TRI sites are facilities that release enough of certain chemicals that they are required to report releases annually to a national database. The study found that most study participants (both with and without MS) lived within 5 miles of a TRI site but that the total amount of chemical release was higher for TRI sites near where children with MS lived compared to TRI sites near children without MS. Additionally, out of the different air pollutants examined, fine particulate matter, carbon monoxide, sulfur dioxide and lead were associated with higher odds for developing pediatric MS. Further research into why these particular pollutants are associated more with MS should be conducted to determine how they interact with the central nervous system differently than other air pollutants and how exposure could be lowered.

What's Known on This Subject: Previous studies have identified air quality as a risk factor of interest in early onset MS but have not explored specific pollutants

What This Study Adds: This study suggests specific pollutants such as fine particulate matter, carbon monoxide, sulfur dioxide and lead were most associated with risk for early onset MS.

Full Manuscript: Lavery A, et al. Urban air quality and associations with pediatric multiple sclerosis. *Annals of Clinical and Translational Neurology*, Epub 2018 Sep 27

Early Exposure to Infections

Manuscript Summary

The purpose of this study was to determine if infectious exposures early in life such as daycare, early use of antibiotics, vaccinations and other germ exposures were associated with MS risk in children. Parents of 832 children with and without MS in the United States completed an environmental questionnaire that captured behaviors in childhood such as pacifier use, thumb sucking, outdoor play and illnesses in the first five years of life such as ear infections and high fever. The findings in this study suggest that these early infections are not associated with developing MS.

What's Known on This Subject: Previous studies of autoimmune diseases have seen a link between disease development and viral infections in the first years of life. Epstein-Barr Virus (EBV) exposure is a recognized factor for MS but little is known about other infections that might contribute to MS if exposed to early in life.

What This Study Adds: The study suggests that exposure to things like daycare, antibiotics, vaccinations, pacifier use, and other types of germs early in life are not associated with an increased risk of developing MS.

Full Manuscript: Mar, S. et al, Early infectious exposures are not associated with increased risk of pediatric-onset multiple sclerosis; *Multiple Sclerosis and Related Disorders*, 2018 May;22 103-107.

RECENT PUBLICATIONS

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4. Nourbakhsh B, Rutatangwa A, Waltz M, et al. Heterogeneity in association of remote herpesvirus infections and pediatric MS. *Annals of Clinical and Translational Neurology*. doi: <https://onlinelibrary.wiley.com/doi/abs/10.1002/acn3.636>. Epub 2018 Sep17
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8. Waubant E, Lotze T. *Pediatric Demyelinating Diseases of the Central Nervous System and Their Mimics*. Switzerland: Springer International Publishing; 2017.
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14. Bourne T, Waltz M, Casper T, et al. Evaluating the association of allergies with multiple sclerosis susceptibility risk and disease activity in a pediatric population. *J Neurol Sci*. 2017;375:371–375.
15. Chitnis T, Graves J, Weinstock-Guttman B, et al. Distinct effects of obesity and puberty on risk and age at onset of pediatric MS. *Annals of Clinical and Translational Neurology*. 2016;3(12):897–907.
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