Issue #2 - 2025

NRXN1 NEWSLETTER

ASPE Study | University of Pennsylvania | Philadelphia, PA

Welcome back!

To the newsletter designed as a place to hold the shared experiences of *NRXN1* gene (2p16.3 deletion)

In our second addition of the *NRXN1* Newsletter, we are eager to update you all on several exciting research updates, ASPE publication breakdowns, helpful resources, and more information on how you can join a *NRXN1* Support Group today!

Since creating this newsletter, we have developed a running list of resources for those with rare genetic disorders -- particularly with a *NRXN1* gene variant (2p16.3 copy number variant). This list of resources can be found on the "Resources" page on our website.

We continue to welcome with open arms any thoughts on how we can better support both this *NRXN1* newsletter, and the community reading it.

Please feel free to reach out via our email (aspe@pennmedicine.upenn.edu) at any time for comments and suggestions regarding this newsletter.

All our best,
The ASPE Study Team

In Today's Edition...

***NRXN1* Needs Assessment: Part 1**

Our Recent *NRXN1* Publications: Explained

Update on the *NRXN1* Family Support Group.

ASPE Team Spotlight: Mike Hart

An Assessment of *NRXN1* Needs: Part 1

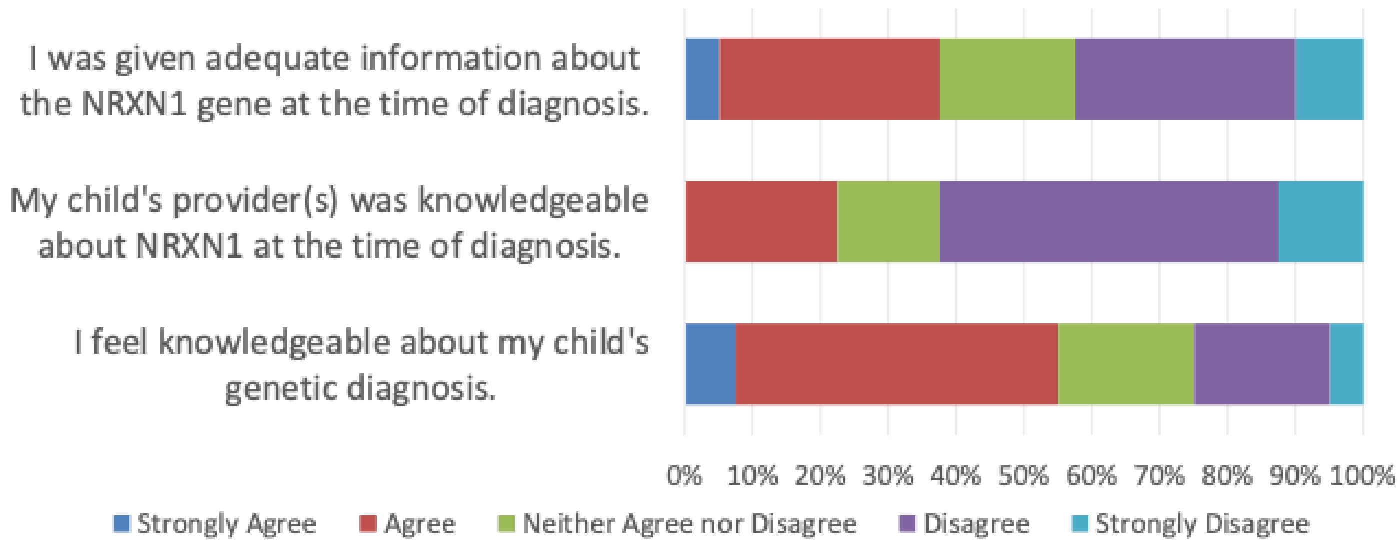
Featuring Brielle Gehringer, Certified Genetic Counselor

Formally a Clinical Research Coordinator on the ASPE Study, Brielle Gehringer, MS, CGC, is now a genetic counselor for the Armellino Center of Excellence for Williams Syndrome (ACE) at the Perelman School of Medicine at the University of Pennsylvania. During her time as a clinical research coordinator here at the Autism Spectrum Program of Excellence, Brielle performed a Needs Assessment of Families with *NRXN1* (2p16.3) Variants as a first step to improving care for *NRXN1* families. As it currently stands, there is little to no published research regarding the needs of the growing *NRXN1* population.

Using a secure database, Brielle and her team distributed surveys to primary caregivers of those with *NRXN1* or 2p16.3 variants. Some of you very may well have been included in this survey distribution! The survey was designed with prompts that assessed these families diagnostic journey, access to services, access to information, satisfaction with care, and impact on the family. In Part One of this *NRXN1* Needs Assessment breakdown, we will be sharing the results regarding Satisfaction with Care & Diagnosis and Care.

Overall, it was found that caregivers were generally satisfied with their child's medical and behavioral healthcare. 72.5% of families saw at least 3 providers while seeking a diagnosis for their child, 29 of 40 families reported no challenges in getting genetic testing, and 26 of 40 families (65%) received genetic counseling regarding their child's diagnosis. Yet, only 53.8% found genetic counseling to be helpful. This low perception of the value of genetic counseling among caregivers is likely related to the limited information available about *NRXN1*.

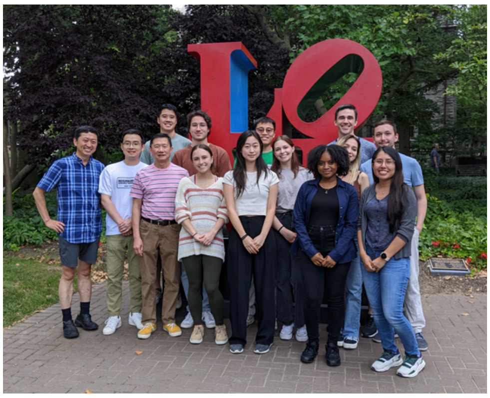
When assessed on Access to Information, caregivers report dissatisfaction with the amount of information given by providers.



In the next *NRXN1* Newsletter, Part II will break down results regarding Access to Information, Sources of Information, and Access to Services. To conclude the breakdown of this *NRXN1* Needs Assessment, we will share additional themes, limitations and next steps for improving the care for the NRXN1 community.

Our Recent *NRXN1* Publication: Explained

Read about the Zhou Lab's recent research paper



The Zhou Lab, lead by Zhaolan "Joe" Zhou, published a paper in early 2023 titled "Allelic contribution of *NRXN1*a to autism-relevant behavioral phenotypes in mice". Animal models are very helpful in experimentally testing the causative effects of gene variants on brain development and behaviors. In this research study, Joe and his lab, supported by the Bucan and Brodkin labs, investigated different deletions (aka tiny missing pieces of DNA) across the *NRXN1* gene in mice to assess autism-related behaviors in animal models. These models are key to better understanding the genetic basis of autism and the ways that the *NRXN1* gene affect brain development and behaviors. Every chromosome contains thousands of genes that hold the important information needed for us to develop and function at best health. A tiny piece of missing material on a chromosome can sometimes disrupt development, but that is not always the case. Identifying when these missing pieces do disrupt development can help us further understand the relationship between autism and *NRXN1*. The Zhou lab's research found that autism-relevant behavioral traits in mice are dependent on the animal's gender and the position of the deletion. Losing one copy of the *NRXN1* gene, producing a similar genetic structure to humans with *NRXN1* deletions and autism, prompts behaviors relevant to autism. These behaviors were most notably social novelty preference and repetitive motor behaviors, which are relevant to two core autism diagnostic domains -(1) impairment in social interaction and (2) restricted, repetitive patterns of behaviors. The Zhou Lab's findings support the importance of sex, genetic structure, and the amount of functional *NRXN1* product in eliciting autism-related behaviors.

Read the full publication here: doi.org/10.1371/journal.pgen.1010659

ASPE Team Spotlight: Mike Hart

Learn about one of the Principal Investigators and his Lab in the ASPE Study....

Michael Hart, Ph.D., is an Assistant Professor of Genetics at the Perleman School of Medicine, and is the Principal Investigator of the Hart Lab. The Hart lab works closely with other ASPE researchers studying the functions of autism-associated genes, including a specific focus on neurexin genes in C.elegans (worms!). The Hart lab mixes neuroscience and genetics to research how genetics involved in autism in humans, but conserved through evolution to worms, can result in changes to behaviors through mechanistic roles at neurons and in neuronal circuits. As neurexin genes have been associated with changes in human behavior and are ancient genes important for all nervous systems, neurexin is a major focus for Dr. Hart and his team. The Hart lab is also studying how neurexin may interact with other autism genes, and how neurexin and many other genes can result in similar and different changes in worm behavior! The Hart lab has uncovered molecular roles for different isoforms of *NRXN1*/nrx-1 in circuits and behaviors. We are also testing how variations in neurexin genes impact specific behaviors and not others. Together this work will expand our understanding of neurexin and variation in gene, with important implications for the *NRXN1* community.

Read more about the Hart Lab at: https://www.mphartlab.com

Update on the 2p16.3/*NRXN1* Family Support Organization

Featuring Marissa Mitchel, ASPE Advisory Board Member

In our last newsletter, you were introduced to Marissa Mitchel and Don Culp, parents of two children with the 2p16.3/*NRXN1* deletion. You learned not only who they are, but about their interest in organizing support for families affected by 2p16.3/*NRXN1* deletions. Since our last edition, Marissa is in the process of obtaining 501(c)3 nonprofit status with her organization, *NRXN1* Network, in order to best serve and support individuals with rare disorders. The mission of the *NRXN1* Network is for families, clinicians, and scientists to build a collaborative network to support individuals affected by *NRXN1* disorder. This network will increase awareness, inform our understanding, and accelerate the diagnosis and treatment of *NRXN1* disorder.

VISIT WWW.NRXN1NETWORK.ORG TO LEARN MORE ABOUT THE *NRXN1* NETWORK!

Marissa has also graciously joined ASPE's Advisory Board to advocate for individuals like her son with rare disorders like the 2p16.3 deletion. We look forward to continuing our collaboration with both Marissa and the *NRXN1* Network as we grow our supports for the community.

If you are interested in helping in any way, or if you would just like to learn more, please feel free to email Marissa at marissa.weyer@gmail.com.

WE ALWAYS WANT TO HEAR FROM YOU!

We continue to welcome with open arms any thoughts on how we can better support both this *NRXN1* newsletter, and the community reading it.
What would make the experience of reading this newsletter most meaningful to you? Is there anything you'd like to hear from us? Are there any principles you'd like to guide our work?

General comments can be emailed at any time to aspe@pennmedicine.upenn.edu.