Ten Areas Where SPARK Increased Our Understanding of Autism

Featuring SPARK's Principal Investigator, Dr. Wendy Chung

What is SPARK?

SPARK is the largest study of autism ever! SPARK has more than 415,000 participants including 175,000 people with ASD and their first-degree family members.

SPARK aims to learn more about autism by recruiting autistic individuals and their families, collecting their behavioral, medical, and genetic data, and connecting them to research opportunities.

- **Over 30 clinical sites** nationwide represent SPARK and help recruit individuals and families affected by autism.
- SPARK has deepened efforts to reach communities traditionally underrepresented in research to ensure that we are capturing the true **diversity of the entire autism community.**
- SPARK adheres to the highest standards of research ethics to **protect your privacy and the security of your data.**

What is SPARK's mission?

1. To better understand the causes of autism and to help improve lives
2. To unite the entire autism research community
3. To provide research opportunities for people from a wide range of backgrounds and experiences
4. To give back to our participants by providing them with answers to their autism questions

SPARK is the largest study of autism ever!

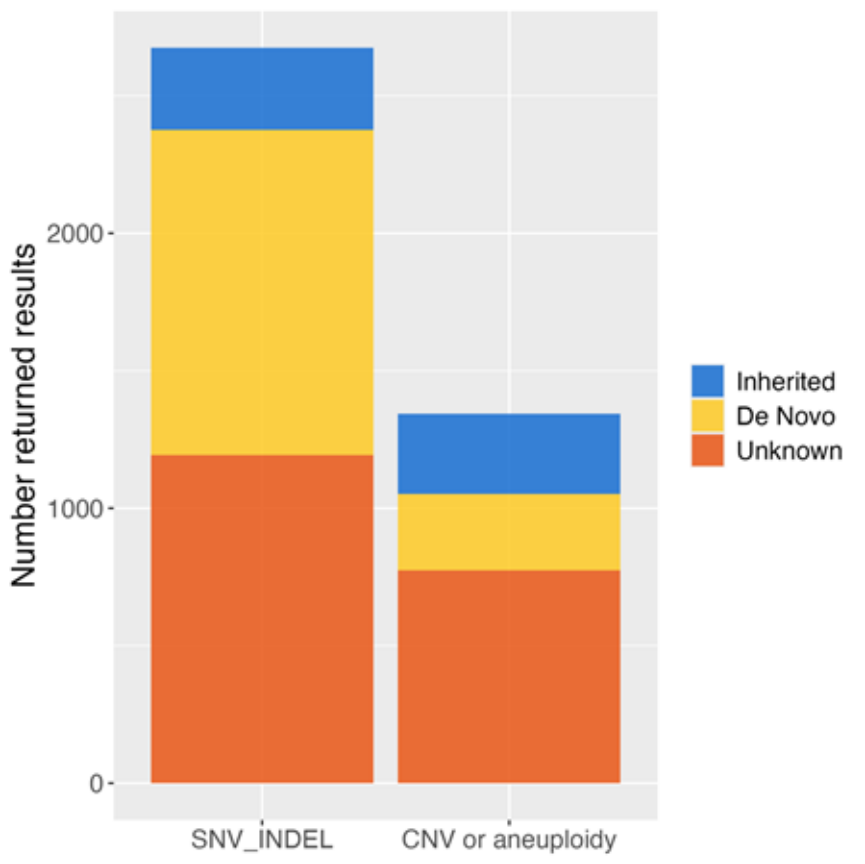
Our community:

- **Over 415,000 participants**, including individuals with autism and their family members
- **Over 175,000** participants with autism
  - **138,000+ children** (<18 years)
  - **37,000+ adults**

Our commitment to research:

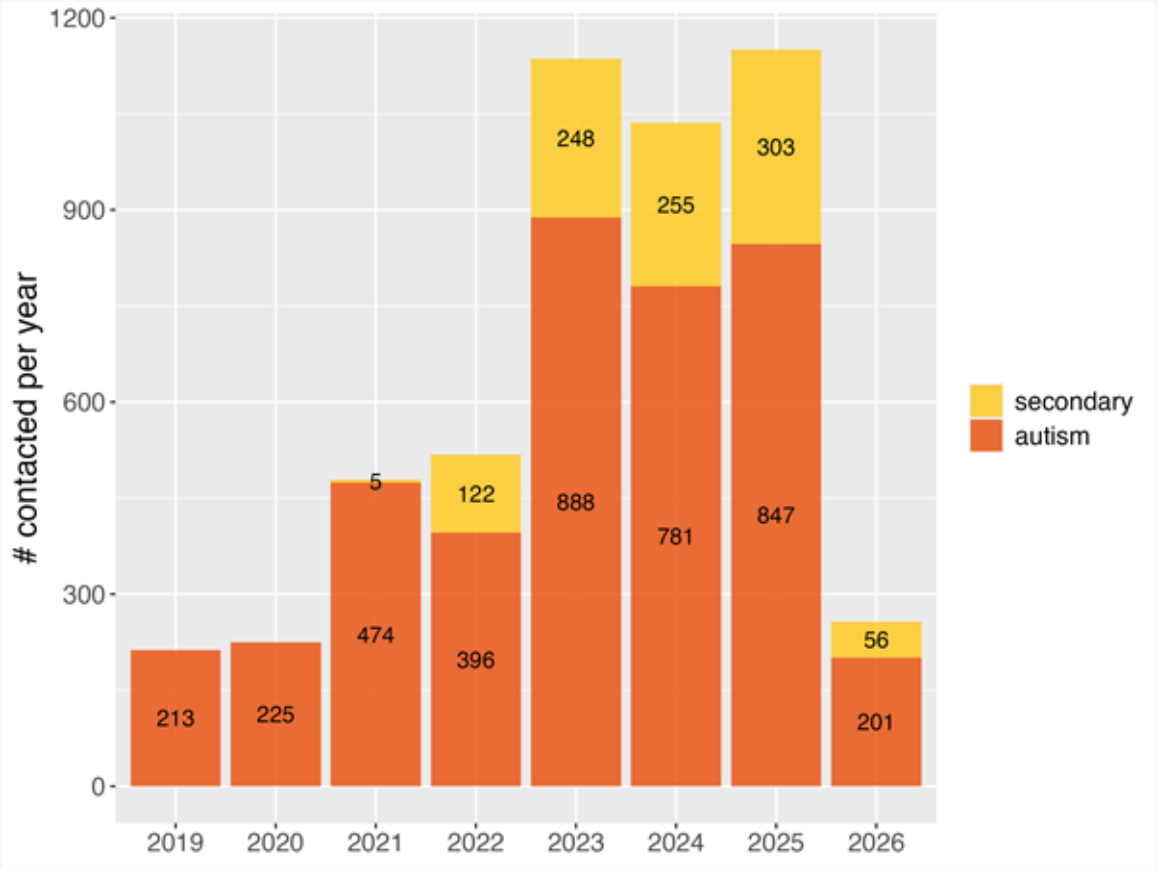
- **Over 450 researchers** have been approved to use SPARK data for their research.
- **Nearly 350 Research Match Studies** have launched, with dozens more in progress.
- **More than 157,500 families have been invited to participate –** often more than once – which has resulted in **nearly 74,500 responses to study invitations.**
- SPARK data have helped discover **more than 100 autism-related genes.**

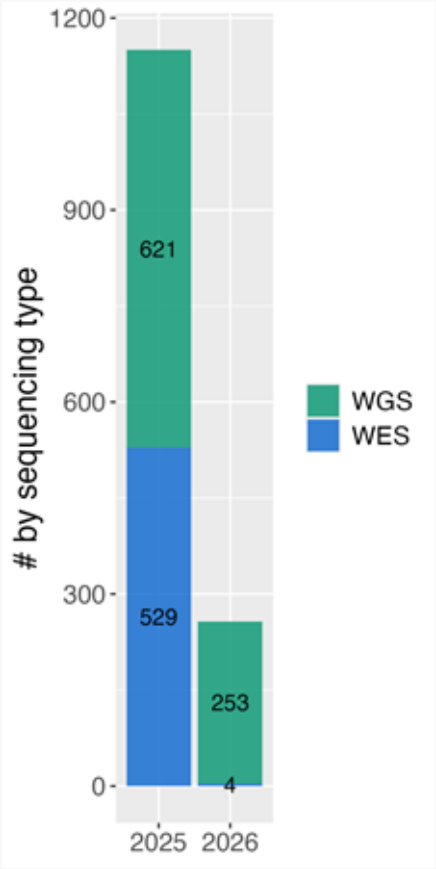
SPARK has contacted more than 4,000 autistic participants about autism genetic findings



- 67% of these results alter a single gene (SNVs). The remaining 33% change stretches of multiple genes on a chromosome (CNV or aneuploidy).
- 36% of all returned results have “de novo” inheritance. Which means the genetic change is new in the person with autism.
- In these cases we are able to confidently test both parents and say the variant is not present in either parent.
- 18% of these results came from whole-genome sequences since the switch in sequencing providers.

Update on Return of Genetic Results





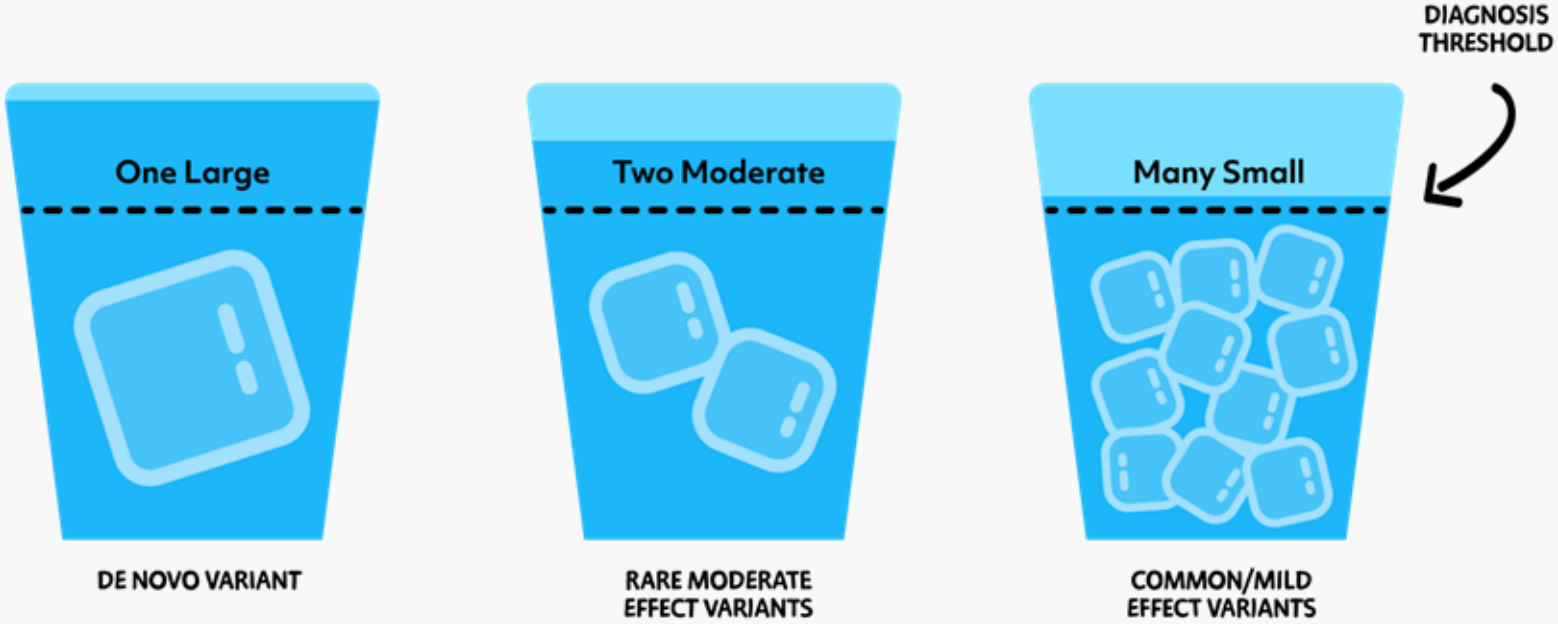
10 Areas Where SPARK Increased Our Understanding of Autism

10 Areas Where SPARK Increased Our Understanding of Autism


1
Accelerated discovery of the genetic causes of autism

Different Genetic Variants, Different Effects

Each person with autism has a unique set of environmental and genetic factors that contribute to their condition.



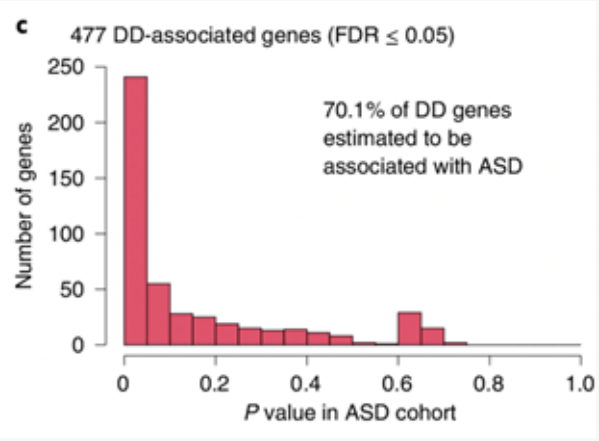
RESEARCH DATA PUBLICATION

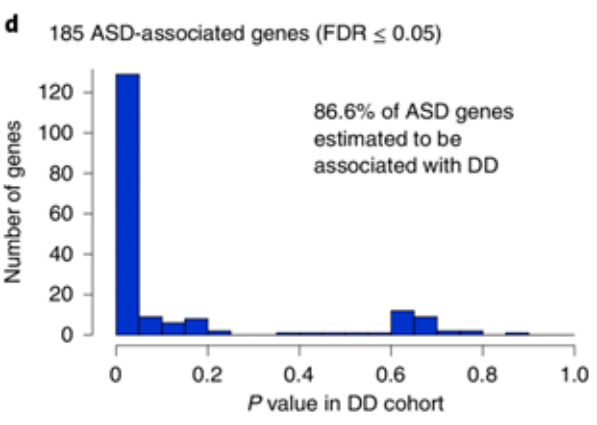
What rare genetic changes can tell us about autism

- Genes in people diagnosed first with developmental delay versus autism are overlapping.
- By looking at when in development neurons use these genes, the study suggests that ASD gene are used later in fetal development. By contrast, genes with stronger links to intellectual disability are used very early in brain development.

Jack M. Fu

Michael Talkowski



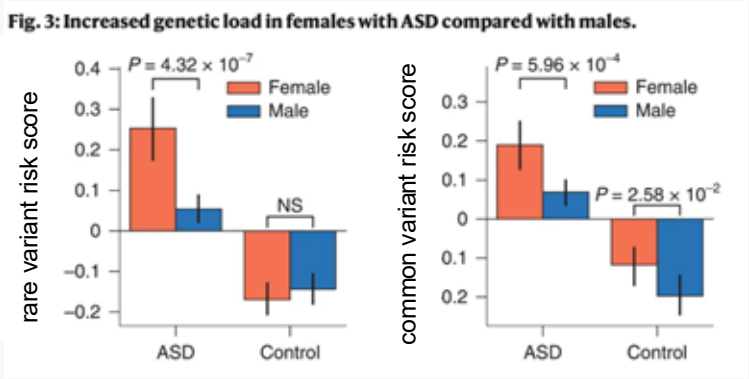


Fu, J.M., Satterstrom, F.K., Peng, M. *et al.* Rare coding variation provides insight into the genetic architecture and phenotypic context of autism. *Nat Genet* **54**, 1320–1331 (2022).

RESEARCH DATA PUBLICATION

How rare variants, polygenic risk, and sex influence autism traits

- Autism results from a combination of types of genetic variants: strong effect variants that appear new (de novo) in the person with autism; moderate effect rare variants that can be transmitted from a parent; and small effect common variants that are common throughout the population and combine to increase the chance that someone has autism.
- The researchers built a prediction score that considers all these genetic factors. Females have more “genetic load” than males, suggesting that it takes more genetic contributions for autism to manifest in females.
- When people with autism have more of the common ‘small’ effect variants, they have less of the ‘strong’ rare ones, and vice versa, supporting that these work together.



Danny Antaki

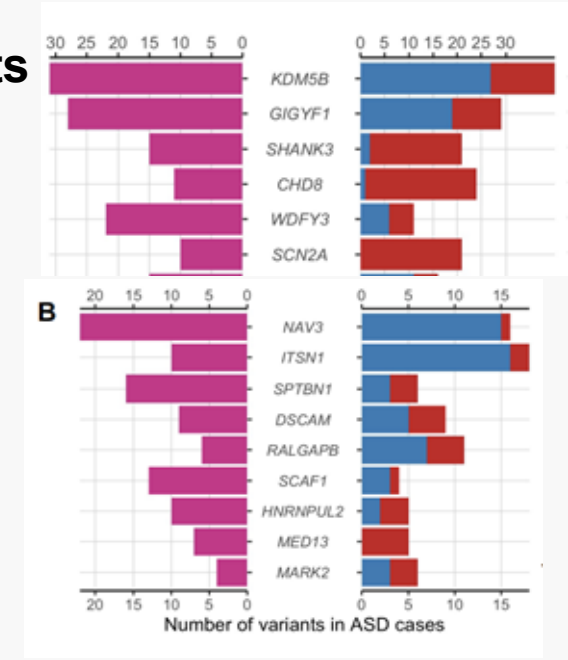
Jonathan Sebat

Antaki, D., Guevara, J., Maihofer, A.X. *et al.* A phenotypic spectrum of autism is attributable to the combined effects of rare variants, polygenic risk and sex. *Nat Genet* **54**, 1284–1292 (2022).

RESEARCH DATA PUBLICATION

Looking at both *de novo* and inherited variants in 42,607 individuals with autism finds a new class of autism genes

- Spontaneous, or *de novo* genetic variants linked to autism were mainly found in already known autism genes. But there is also a new group of genes that contribute to autism.
- The study's large size allowed researchers to identify 5 of these genes that have moderate effects. (*NAV3*, *ITSN1*, *MARK2*, *SCAF1* and *HNRNPUL2*)
- There are more genes like this involved in autism, but even larger numbers of autism participants are needed to find them.



Xueya Zhou

Pamela Feliciano

Wendy Chung

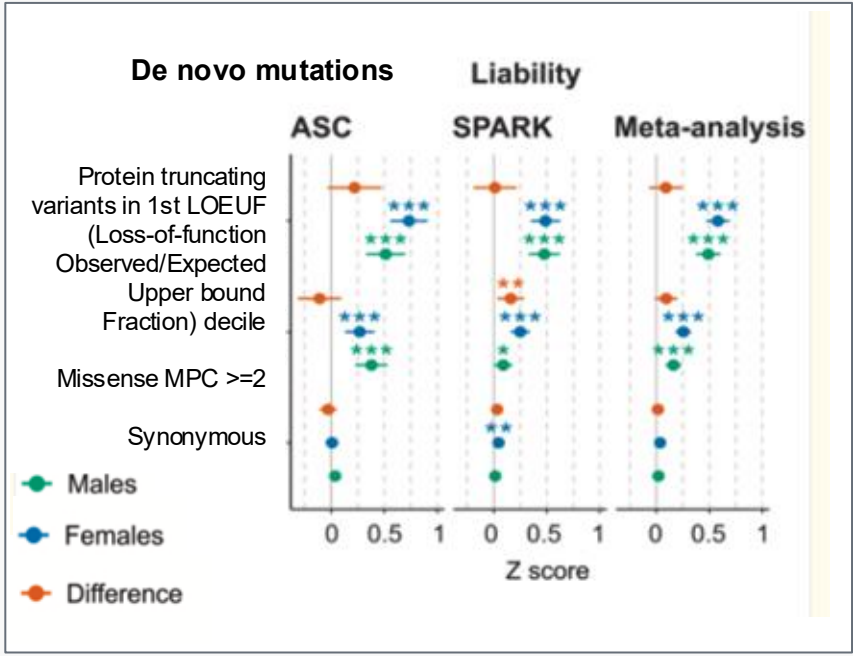
Zhou, X., Feliciano, P., Shu, C. *et al.* Integrating de novo and inherited variants in 42,607 autism cases identifies mutations in new moderate-risk genes. *Nat Genet* **54**, 1305–1319 (2022).

Gained insights into difference between boys and girls

RESEARCH DATA PUBLICATION

Looking at the effect of variants on autism risk in males and females

- This work combines genetic data from SPARK and the autism sequencing consortium for 21,501 autistic individuals and 9,223 sibling controls.
- The researchers looked at how much certain variants contribute to an individual having autism, a calculation called liability. They compared *de novo* and rare variants in females and males and in participants with and without cognitive delay.
- The study suggests that *de novo* and rare variants have the same impact on autism in females as in males. This is true even in genes differentially expressed in the male brain during development.
- This supports the threshold model, which says that it takes more variants to lead to an autism diagnosis in females than in males, rather than the variants themselves having a larger effect, AKA liability, in males.



Mahmoud Koko

Hillary Martin

Koko, M., Satterstrom, F. K., Autism Sequencing Consortium, APEX consortium, Warrier, V., & Martin, H. (2025). Contribution of autosomal rare and de novo variants to sex differences in autism. American journal of human genetics, 112(3), 599–614.

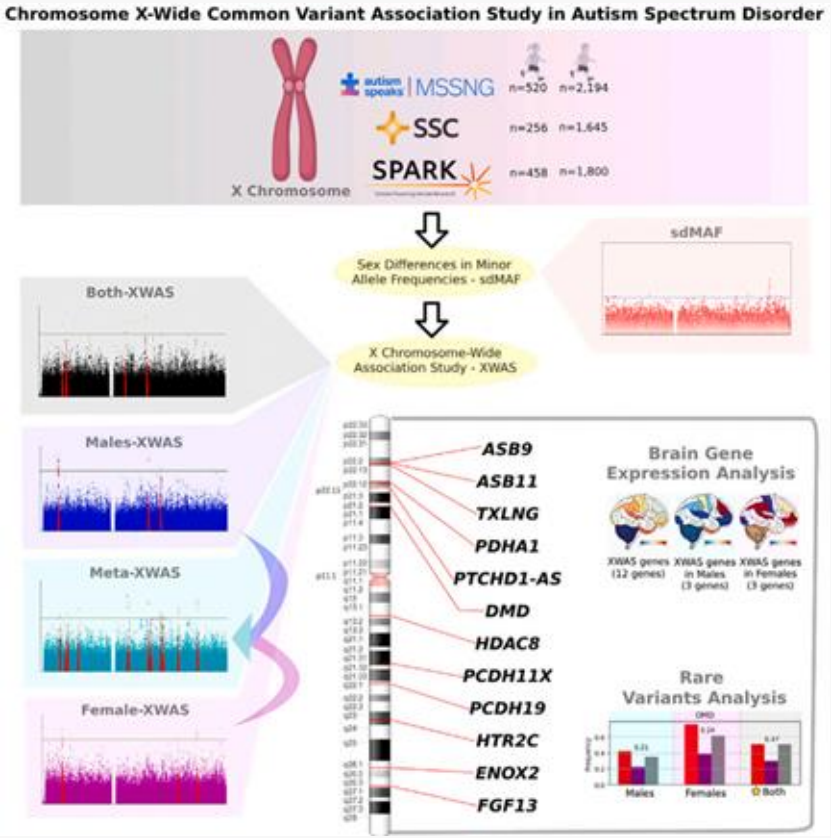
RESEARCH DATA PUBLICATION

Chromosome X-wide common variant association study in autism spectrum disorder

- A common variant association study specific to the X chromosome, called XWAS, using whole genomes from 6,873 autistic individuals from multiple cohorts including SPARK.
- The study finds 59 variants associated with ASD implicating 91 genes, of which 17 show a significant association with autism, including DMD and PTCHD1-AS.
- The 12 autism genes with expression data show upregulation in the cerebellum during fetal development.

Marla Mendes

Stephen Scherer

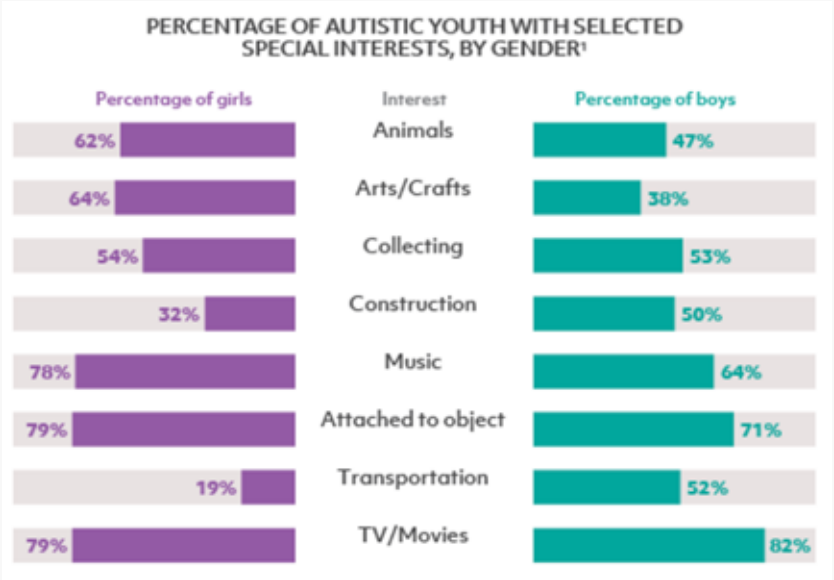


Mendes, M., Chen, D. Z., et al 2025). Chromosome X-wide common variant association study in autism spectrum disorder. *American journal of human genetics*, *112*(1), 135–153.

RESEARCH MATCH STUDY

More similar than different: Characterizing special interests in autistic boys and girls based on caregiver report

- Using a new tool, the Special Interests Survey, researchers surveyed 1,921 autistic boys and girls, ages 2 through 17
- Boys and girls shared three of the top five interests: TV and movies, being attached to objects, and music.
- More boys were interested in construction and mechanical things. Girls were more likely to be interested in animals and arts and crafts.
- Autistic boys and girls had many of the same interests, but they differ on some interests that are traditionally associated with one gender over the other.



Cynthia Brown

Kerri Nowell

Brown CE, Bernardin CJ, Beauchamp MT, Kanne SM, Nowell KP. More similar than different: Characterizing special interests in autistic boys and girls based on caregiver report. Autism Res. 2024 Nov;17(11):2333-2345.

Returned 1,000s of genetic results

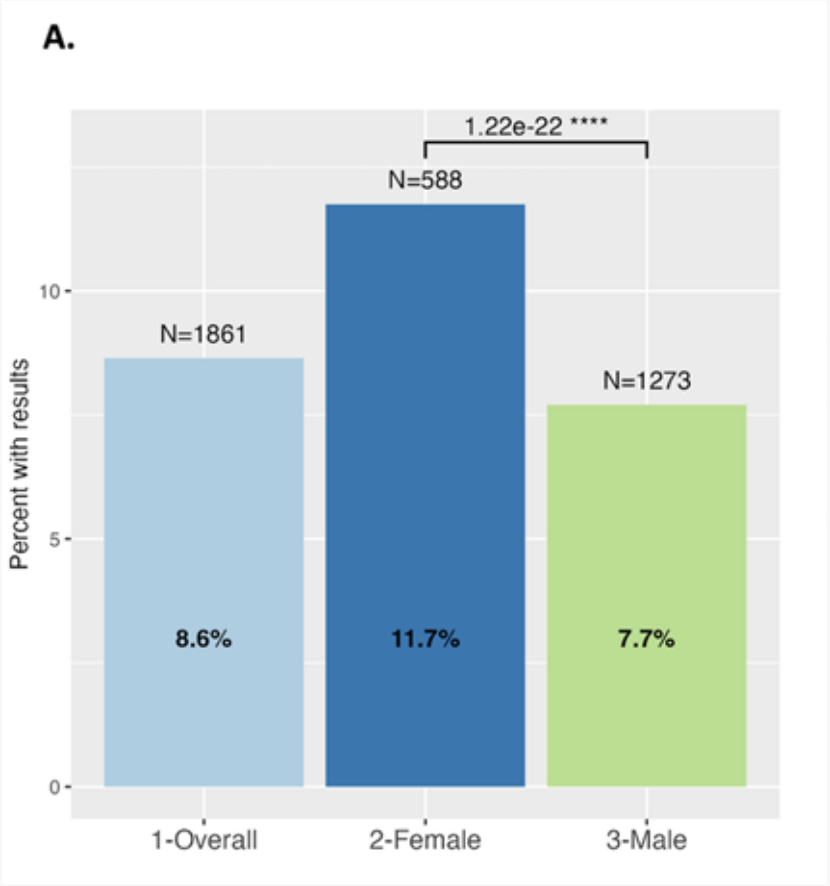
RESEARCH DATA PUBLICATION

Return of genetic research results in 21,532 individuals with autism

- 8.6% of SPARK participants carry a genetic variant linked to autism that SPARK can confidently say was a cause of the condition (returnable result).
- This rate is higher in females than in males.

Jessica Wright

Pamela Feliciano



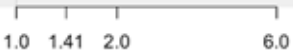
Wright J.R. et al. Return of genetic research results in 21,532 individuals with autism. Genet Med, 2024, Oct.

RESEARCH DATA PUBLICATION

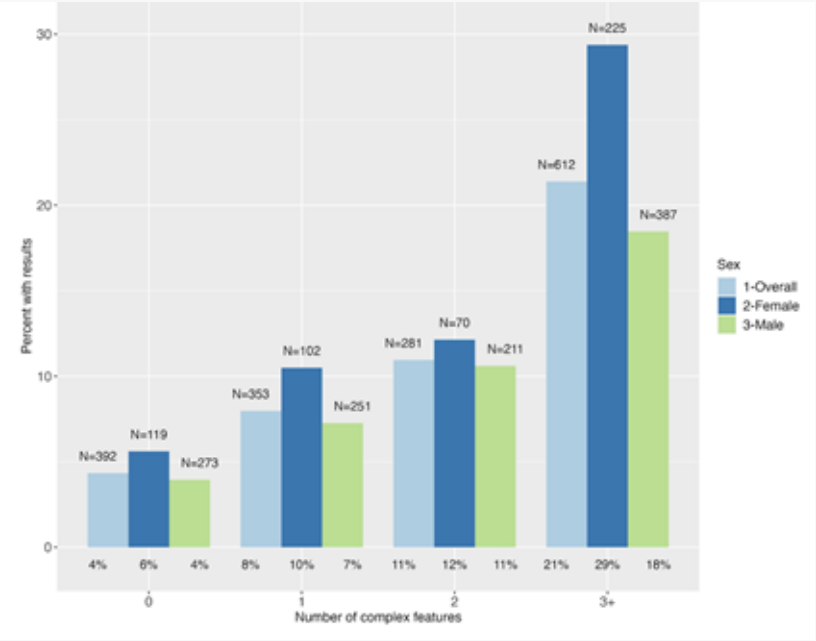
Return of genetic research results in 21,532 individuals with autism

Medical features increase the odds ratio (OR) that a participant will have a returnable genetic result in SPARK

Characteristic	OR	p value (corr.)
Cognitive delays med. cond.	2.4	3.8e-17
Birth defects	2.6	7.1e-14
Cognitive impairment	3.2	4.0e-107
Learning disability	2.1	4.0e-37
Motor delay	3.1	4.2e-82
Encopresis	2.3	2.5e-22
Enuresis	2.2	9.7e-22
Difficulty gaining wt	2.2	2.5e-12
Macrocephaly	2.6	3.0e-13
Microcephaly	4.7	3.1e-16
Short stature	3.5	3.4e-22
Seizure disorder	2.7	5.6e-29
Deafness	2.6	5.1e-11
Strabismus	3.3	1.0e-23



The genetic yield is 21% overall (29% in females) in SPARK participants who endorse 3 or more medical features.



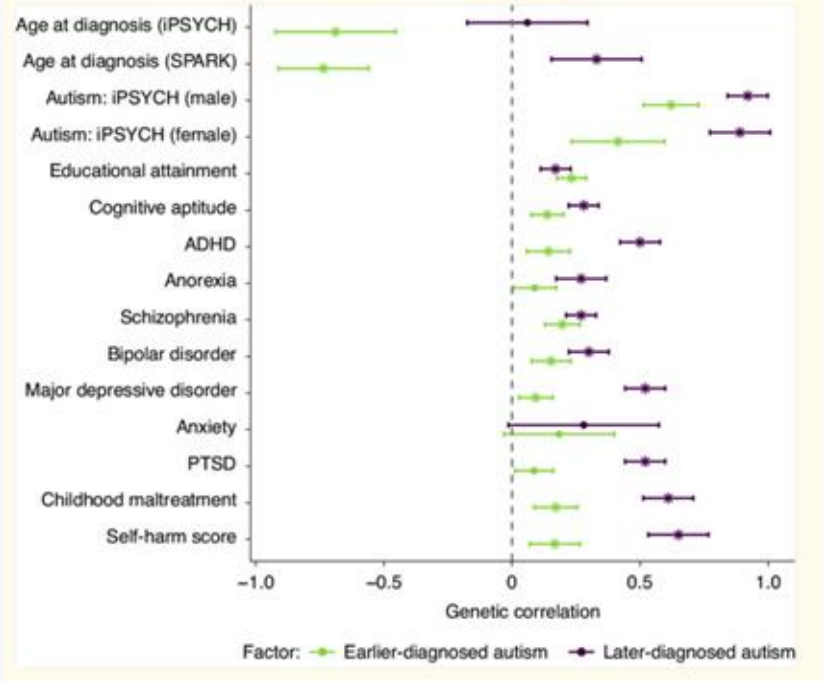
Wright J.R. et al. Return of genetic research results in 21,532 individuals with autism. Genet Med, 2024, Oct.


4
Explored how data can be used to define autism subtypes

RESEARCH DATA PUBLICATION

Autism has different genetic and developmental profiles based on age at diagnosis

- Autism diagnosed earlier in life has a distinct profile from autism diagnosed later, based on phenotype data from 3 birth cohorts.
- Group 1 is earlier autism diagnosis with lower social and communication abilities in early childhood. Group 2 is later autism diagnosis with ADHD and mental-health conditions.
- Using genetic data from SPARK and other large cohorts, researchers associated a distinct genetic profile of common variants (polygenetic risk score) to each group.
- Overall, genetics underlies 11% of the variation in diagnosis age.
- One assumption has been that autism is diagnosed later when it is milder and/or access to diagnosis resources was limited. The new study suggests that some children diagnosed later may have distinct genetic contributions.



Xinhe Zhang

Varun Warrier

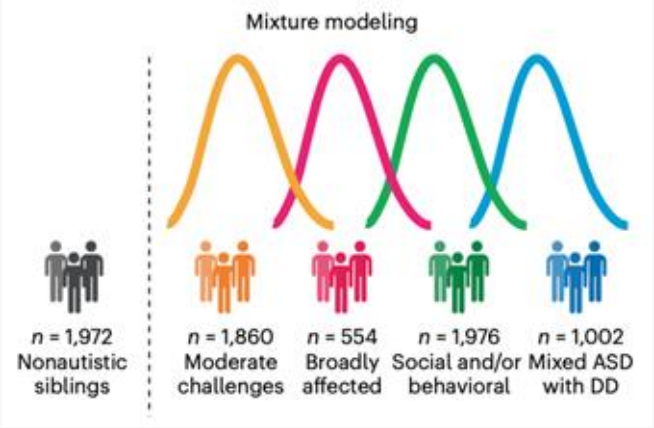
Hillary Martin

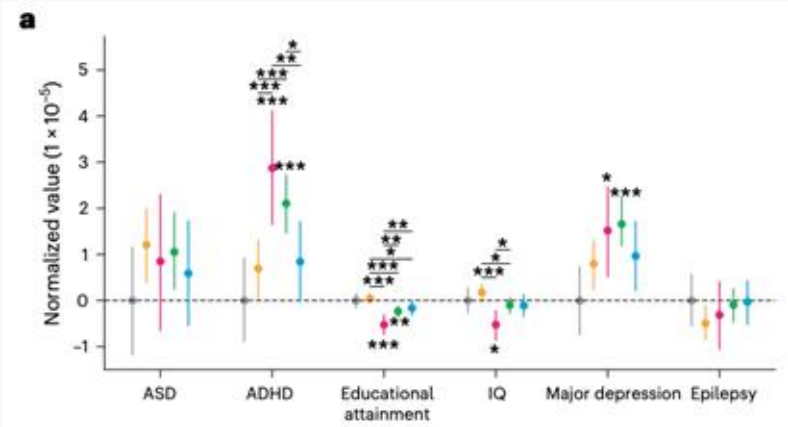
Zhang X, Grove J, et al. Polygenic and developmental profiles of autism differ by age at diagnosis. Nature. 2025 Oct;646(8087):1146-1155.

RESEARCH DATA PUBLICATION

Autism may have 4 different subgroups with different genetics

- Using data from more than 5,000 participants in SPARK and machine learning, researchers found 4 distinct classes of autism: moderate challenges, broadly affected, social and/or behavioral and mixed ASD with developmental delay
- Researchers found some significant differences between the groups in the types and categories of genetic variants.
- Study suggests some differences in biology underlying each category.





Aviya Litman

Natalie Sauerwald

Olga Troyanskaya

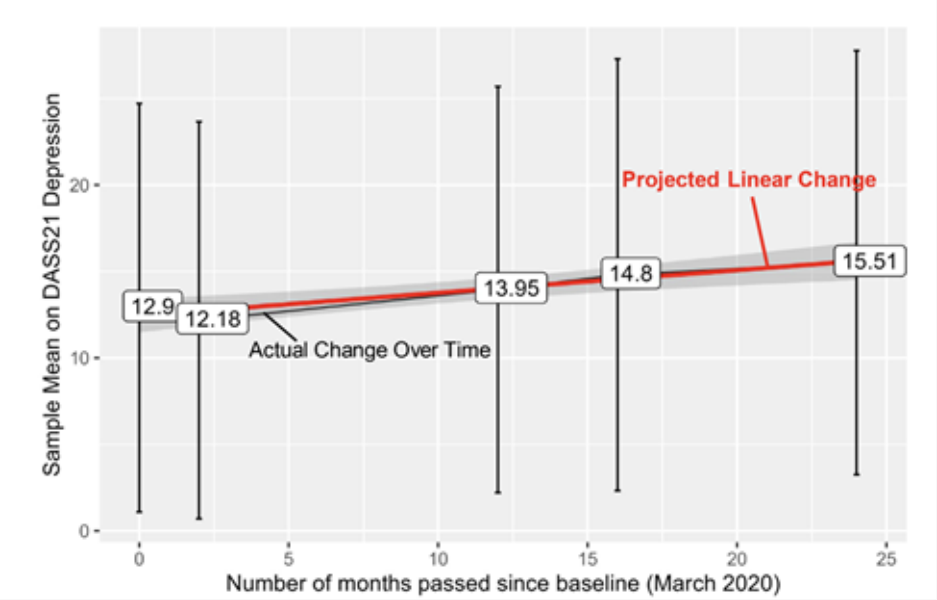
Litman, A., Sauerwald, N., et al (2025). Decomposition of phenotypic heterogeneity in autism reveals underlying genetic programs. *Nature genetics*, *57*(7), 1611–1619.


5
Helped understand autistic adult health outcomes as they age

RESEARCH MATCH STUDY

Patterns and correlates of two-year changes in depressive symptoms for autistic adults

- Over a two-year period, autistic adults reported an increase in depressive symptoms.
  - Individuals with a prior history of depression and lower income reported more depressive symptoms.
  - Those engaged in work and school had lower symptoms.
- These findings suggest ways to help treat depression in autistic adults, including improving access to jobs and education, keeping track of symptoms, and addressing mental health challenges for those with lower incomes.



Shuting Zheng

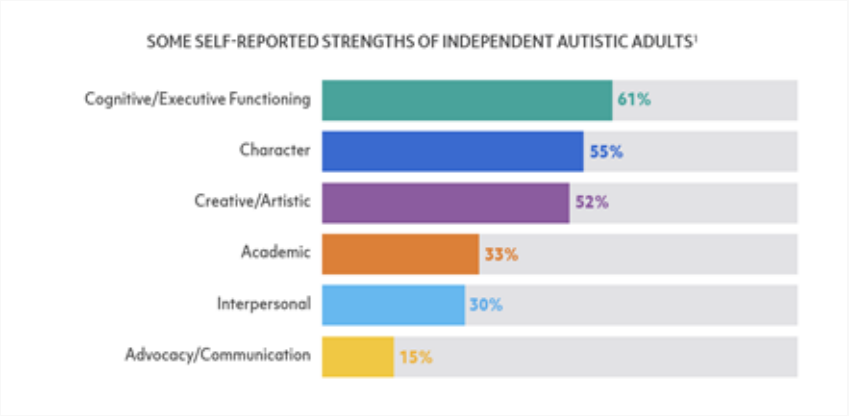
Somer Bishop

Zheng, S et al. Patterns and correlates of two-year changes in depressive symptoms for autistic adults. Frontiers in Psychiatry. 2024 Dec.

RESEARCH MATCH STUDY

Self-reported strengths and talents of autistic adults

- Autistic adults reported a wide range of personal strengths and talents, including attention to detail, strong memory, creativity, honesty, deep focus, and expertise in areas of interest.
- Many strengths were closely tied to core autistic traits, suggesting that characteristics framed as deficits may actually be assets.
- Participants described strengths as meaningful to their identity, well-being, and sense of purpose.
- These findings highlight the importance of strength-based approaches in research, clinical practice, education, and employment settings, rather than focusing solely on challenges or impairments.



Linnea Lampinen

Vanessa Bal

Lampinen, L. A., Singer, J., Wang, X., VanHook, B., Wilkinson, E., & Bal, V. H. (2026). Self-reported strengths and talents of autistic adults. *Autism*, *30*(1), 37-48.

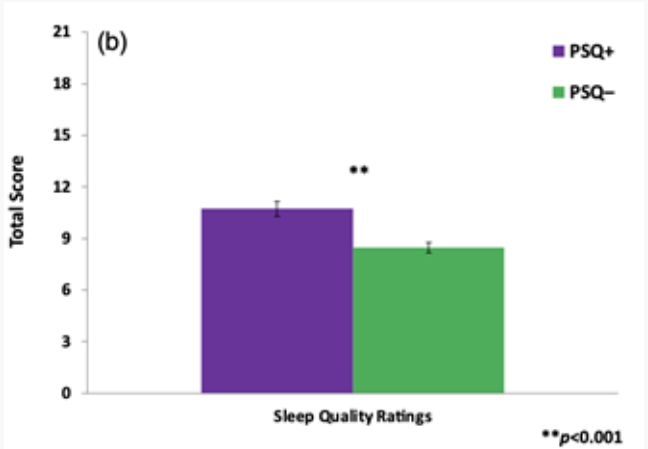
RESEARCH MATCH STUDY

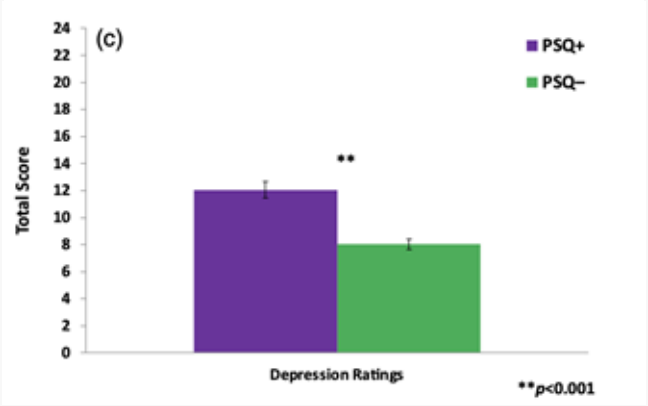
Parkinsonism symptoms linked to social, physical, and mental health in middle and older adulthood (40-83 yr)

- Autistic individuals who screened positive for parkinsonism reported negative impacts on their quality of life, including more memory problems, poorer sleep, and higher rates of depression symptoms.
- This study adds to the growing evidence of a core motor phenotype of autism. It is the first study looking at the impact of parkinsonism symptoms on mental health and quality of life.

Gregory Wallace

Goldie McQuaid





(PSQ=Parkinsonism Screening Questionnaire)

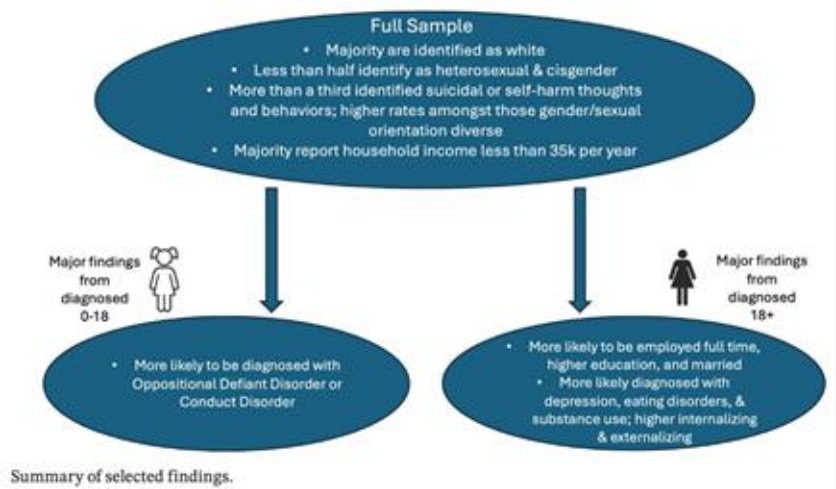
Wallace, G. et al. Elevated parkinsonism symptoms in autism during middle and older adulthood are linked with psychosocial, physical health, and mental health outcomes. Autism Research. 2024 Jun.

Deepened our understanding about autistic women

RESEARCH DATA PUBLICATION

Comparing the Life Experiences of Autistic Women: Childhood vs. Adulthood Diagnosis

- Researchers examined the life experiences of 1,424 autistic adult women based on whether they were diagnosed as children (average age 9.6) or adults (average age 31.8)
- Participants reported typical adult milestones: over 80% had some college education, more than half were employed, and more than half were married or in a romantic relationship.
- Adult-diagnosed women were more likely to work full time than those diagnosed as children.
- High rates of co-occurring mental health conditions in women diagnosed in adulthood suggest that later diagnosis is linked to poorer mental health outcomes



Summary of selected findings.

Maire Claire Diemer

Laura Carpenter

Diemer MC, Ros-Demarize R, et al. Comparative Analysis of Autistic Women Across the Lifespan: Childhood vs. Adulthood Diagnosis. Autism Res. 2025 Aug;18(8):1651-1663.

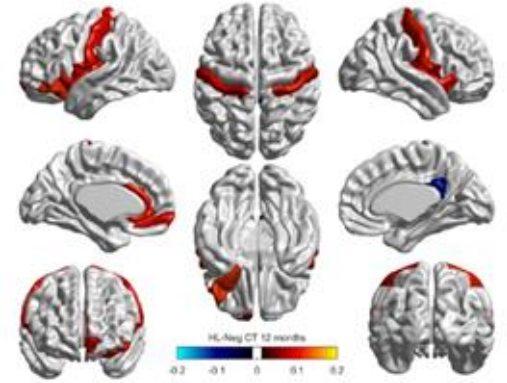
7

Discovered brain-language links are more complex than previously thought by studying baby siblings

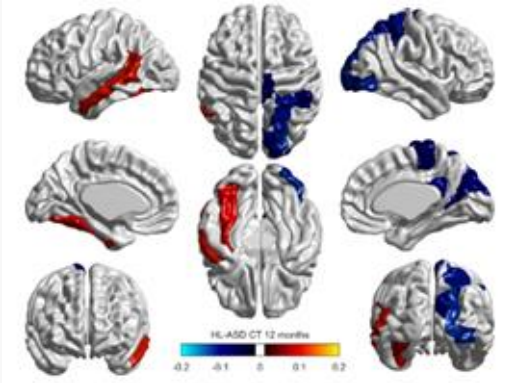
RESEARCH MATCH STUDY

Brain structure in babies later diagnosed with autism is connected to later language development

- Early brain structure at 6 and 12 months predicted language ability at age two.
- Many regions across the brain contributed to language development.
- Some brain measurements were associated with better language skills, while others were associated with language deficits.
- The differences in early brain structure detected by MRI may help identify children during infancy with an increased likelihood of autism.



High-likelihood siblings (NOT diagnosed later)



High-likelihood siblings (Later diagnosed with autism)

MRI measuring cortical thickness (CT) at 12 months
Red=areas of the brain positively associated with language development
Blue=areas of the brain negatively associated with language development

Luke Moraglia

Meghan Swanson

Moraglia LE, Weigman B, Abdi H, et al; IBIS Network. Brain Morphometry in Infants Later Diagnosed With Autism is Related to Later Language Skills. Hum Brain Mapp. 2025 May;46(7):e70221. doi: 10.1002/hbm.70221. PMID: 40348602; PMCID: PMC12063482.


8
Enhanced ability to predict behavioral outcomes in children

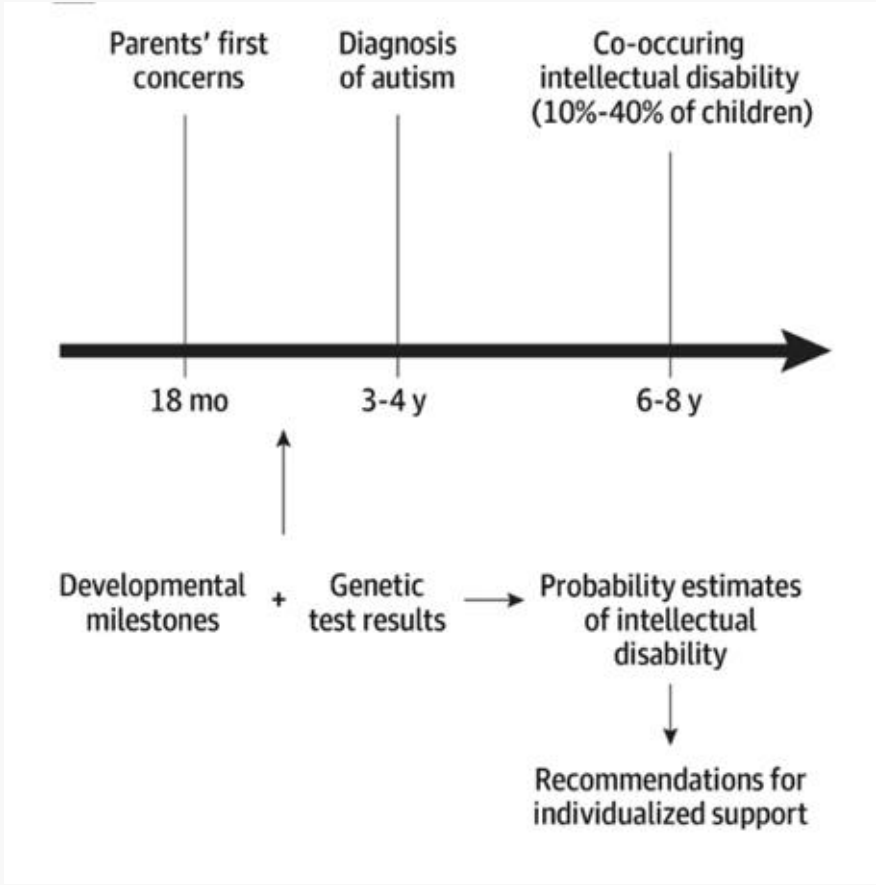
RESEARCH DATA PUBLICATION

Predicting cognitive development at an early age

- This study aims to create a method to predict later development of intellectual disability in children as young as 18 months of age.
- The researchers created a model using genetic and phenotypic data from 5,633 autistic participants in SPARK, the SSC and MSSNG.
- Combining genetic risk scores, rare variants and developmental milestones, such as age of walking, accurately predicts future ID in 10% of the 1,159 participants with an ID diagnosis.

Vincent-Raphael Bourque

Sebastian Jacquemont



Bourque V.R. et al. Genomic and Developmental Models to Predict Cognitive and Adaptive Outcomes in Autistic Children. JAMA Pediatr., 2025

9

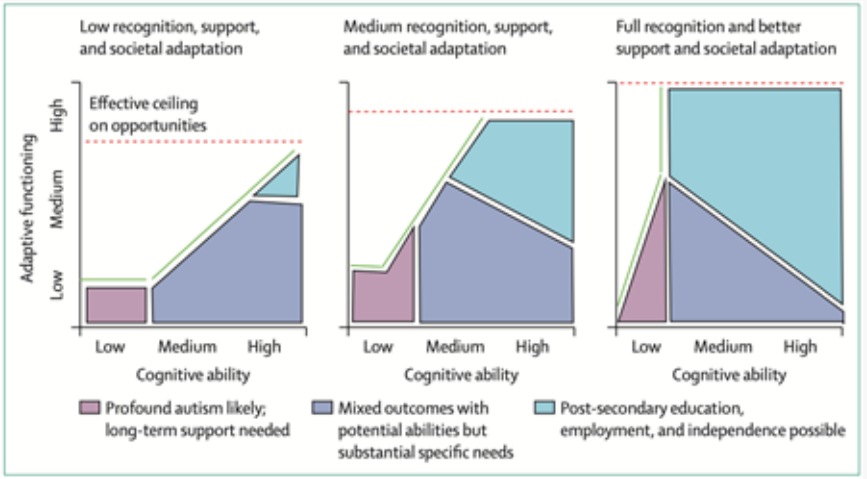
Gained a more in-depth view of profound autism

EXTERNAL PUBLICATION

The Lancet Commission on the future of care and clinical research in autism

- "Profound autism" defined:
  - Is at least 8 years old
  - Requires **24-hour access** to a caretaker
  - Has an **IQ of less than 50** and/or is **non-speaking** or has minimal verbal ability

- Profound autism individuals in SPARK can be identified with variables that indicate:
  - Age at the time of registration
  - The participant requires very substantial support for day-to-day living
  - Speaks no words or single words



Cathy Lord

Tony Charman

Lord, C., Charman, T., et al.. (2022). The Lancet Commission on the future of care and clinical research in autism. *Lancet (London, England)*, *399*(10321), 271–334.

RESEARCH MATCH STUDY

Associations between Social Experiences and Psychological Health for Autistic Youth with Low IQ

- Low rates of social participation were reported.
- Having social needs met was associated with lower depressive symptoms and increased quality of life
- These findings suggest that promoting positive social experiences and ameliorating negative ones might be an avenue to improving psychological health in this group.

Table 2: Frequency of responses to social participation questions among parents of youth with autism and low IQ

	Amount - % (n)			Evaluation - % (n)		
Variable	Never	Sometimes (less than once a week)	Frequent (once a week or more)	About the right amount of time	Too little time	Too much time
Spend time with family members	0.7% (2)	19.8% (53)	79.5% (213)	76.5% (205)	15.7% (42)	7.8% (21)
Spend time with friends	38.8% (104)	34.0% (91)	27.2% (73)	54.1% (145)	43.7% (117)	2.2% (6)
Talk on the phone or text with friends	61.9% (166)	16.0% (43)	22.0% (59)	67.5% (181)	29.1% (78)	3.4% (9)
Email, chat online, play videogames with friends	70.9% (190)	11.9% (32)	17.2% (46)	63.1% (169)	32.5% (87)	4.5% (12)
Go to social events (community groups, birthday party, etc.)	20.1% (54)	67.9% (182)	11.9% (32)	52.6% (141)	37.3% (100)	10.1% (27)

Julie Lounds Taylor

Ryan Adams

Taylor JL et al. Associations between Social Experiences and Psychological Health in Autistic Youth with Low IQ. Journal of Autism and Developmental Disorders. 2024 May.

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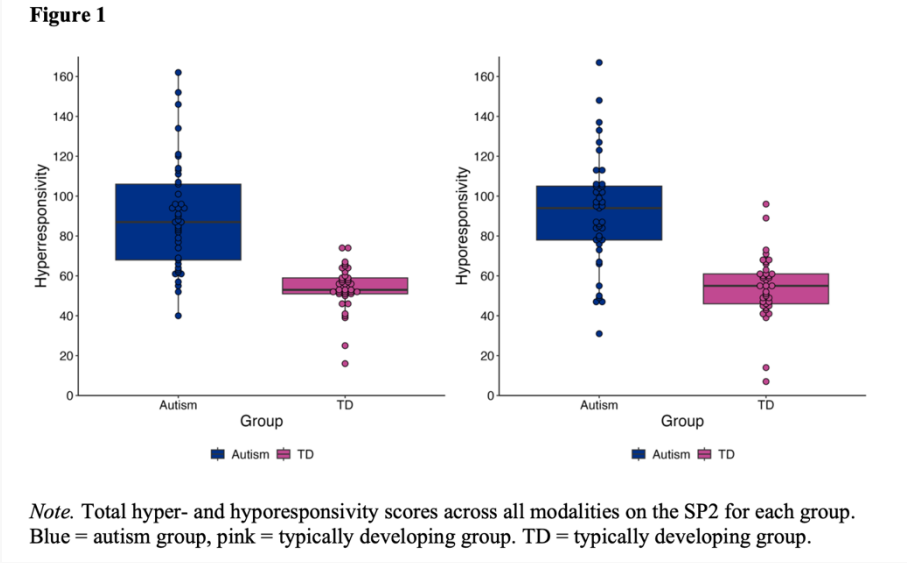
Increased awareness of sensory issues

RESEARCH MATCH STUDY

The Sensory Paradox: Feeling Too Much and Too Little at the Same Time

- The study showed a very strong relationship between being over and under reactive to sensory stimuli (e.g light, sound, and touch).
- Children who were hypersensitive were also more likely to be hypo-sensitive. This was true for autistic and non-autistic children.
- Sensory differences, both hyper and hypo, were associated with challenges in communication, social interaction, and learning ability.
- These findings support a new framework, the “Sensory Paradox.” Both reactions are part of the same underlying sensory processing differences.



Note. Total hyper- and hyporesponsivity scores across all modalities on the SP2 for each group. Blue = autism group, pink = typically developing group. TD = typically developing group.

Kyle Takach

April Levin

Takach KE, Dunham-Carr K, et al. The "Sensory Paradox": Exploring the Positive Association Between Hyper- and Hypo-Responsivity to Sensory Stimuli in Autism and Beyond. medRxiv [Preprint]. 2025 Sep 22:2025.09.21.25336283. doi: 10.1101/2025.09.21.25336283. PMID: 41040683; PMCID: PMC12486020.

Looking toward the road ahead

Connecting you to more research opportunities

SPARK Research Match connects members of the SPARK community to other exciting autism research studies. Participants get the chance to be represented in research and hear about studies that are appropriate for them. And, **we can all learn more about autism.**

SPARK participants are eligible for Research Match! To increase your eligibility:

- Complete your dashboard surveys
- Send in your saliva kits

Participation is always voluntary!

You may receive information about the study from the study team itself. In addition, SPARK will often prepare a Research Match Summary Report and an article about the study.

How SPARK Research Match Works

What's next for SPARK?

As we look at the road ahead for SPARK, our participants remain the driving force of the work we do.

In the years to come, we aim to:

- **Increasing number of researchers** using SPARK data.
- **Continued expansion of outreach and engagement** in the autism communities
- **Remain a trusted source** of information and guidance for autism

Privacy remains at the heart of SPARK!

Continue to share your autism journey with SPARK!

Log into your dashboard.
Complete your surveys.

The more you share, the closer we get to answers.

Autism research needs your SPARK!