

DYRK1A AND AUTISM SPECTRUM DISORDER

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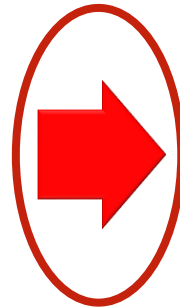
2018 DYRK1A Family Meetup, July 14

THANK YOU!
WE COULD NOT DO THIS RESEARCH
WITHOUT YOU AND WE DO IT FOR YOU!



Genotype

the genetic
makeup of a
person

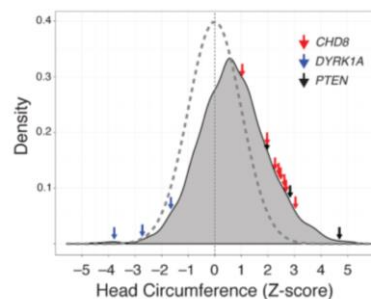


Phenotype

what can be
observed
physically and
behaviorally



HISTORY OF *DYRK1A* RESEARCH



O'Roak et al, 2012



Ji et al, 2015



Van Bon et al, 2016

Ongoing case studies and molecular studies across the world

1997-2012

Small case studies in US, Europe, and Japan

Bronicki et al, 2015



Earl et al, 2017



OUR RESEARCH AT UNIVERSITY OF WASHINGTON

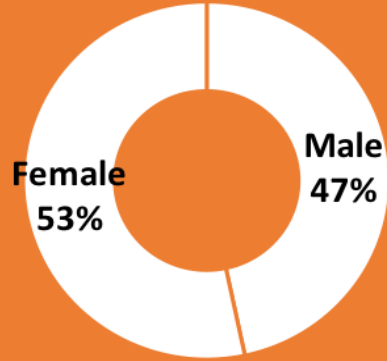
- The Investigation of Genetic Exome Research (TIGER) study
- Study of individuals with *DYRK1A* and other autism-associated mutations
 - 16 different genes in total, including *DYRK1A*
 - Our funding comes from 2 grants from the National Institute of Mental Health (NIMH)
- Brain and behavior patterns in people with these rare mutations
 - Behavioral testing
 - EEG (brain scan)
 - Medical Exam

YOU'VE HELPED US COVER A LOT
OF GROUND IN FIVE YEARS!

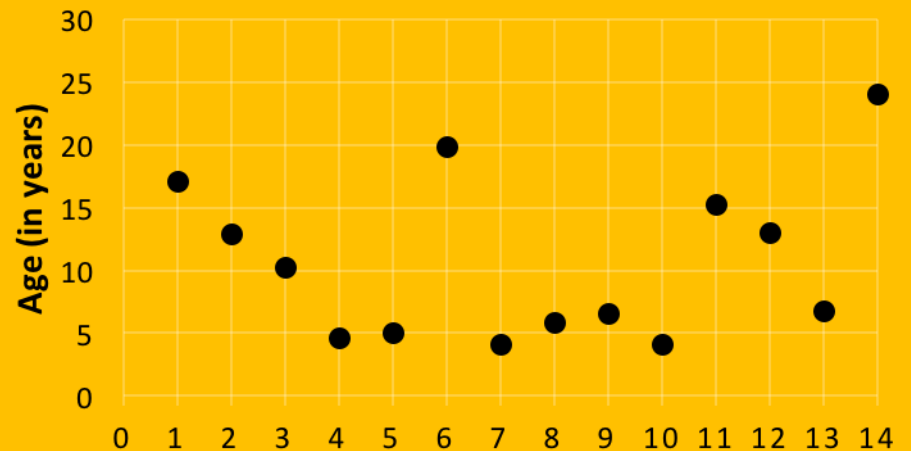


TIGER STUDY DYRK1A DEMOGRAPHICS

GENDER

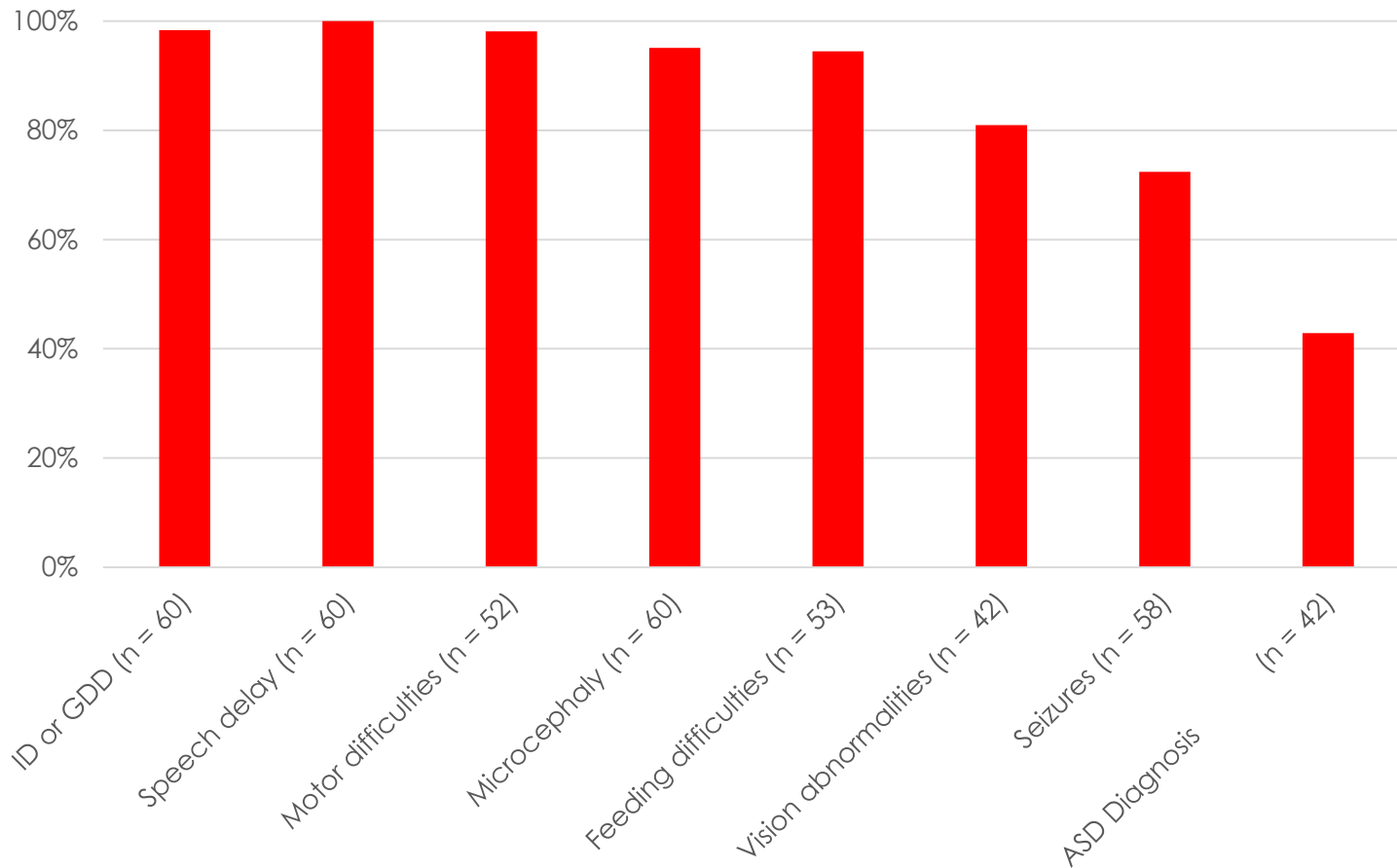


AGE



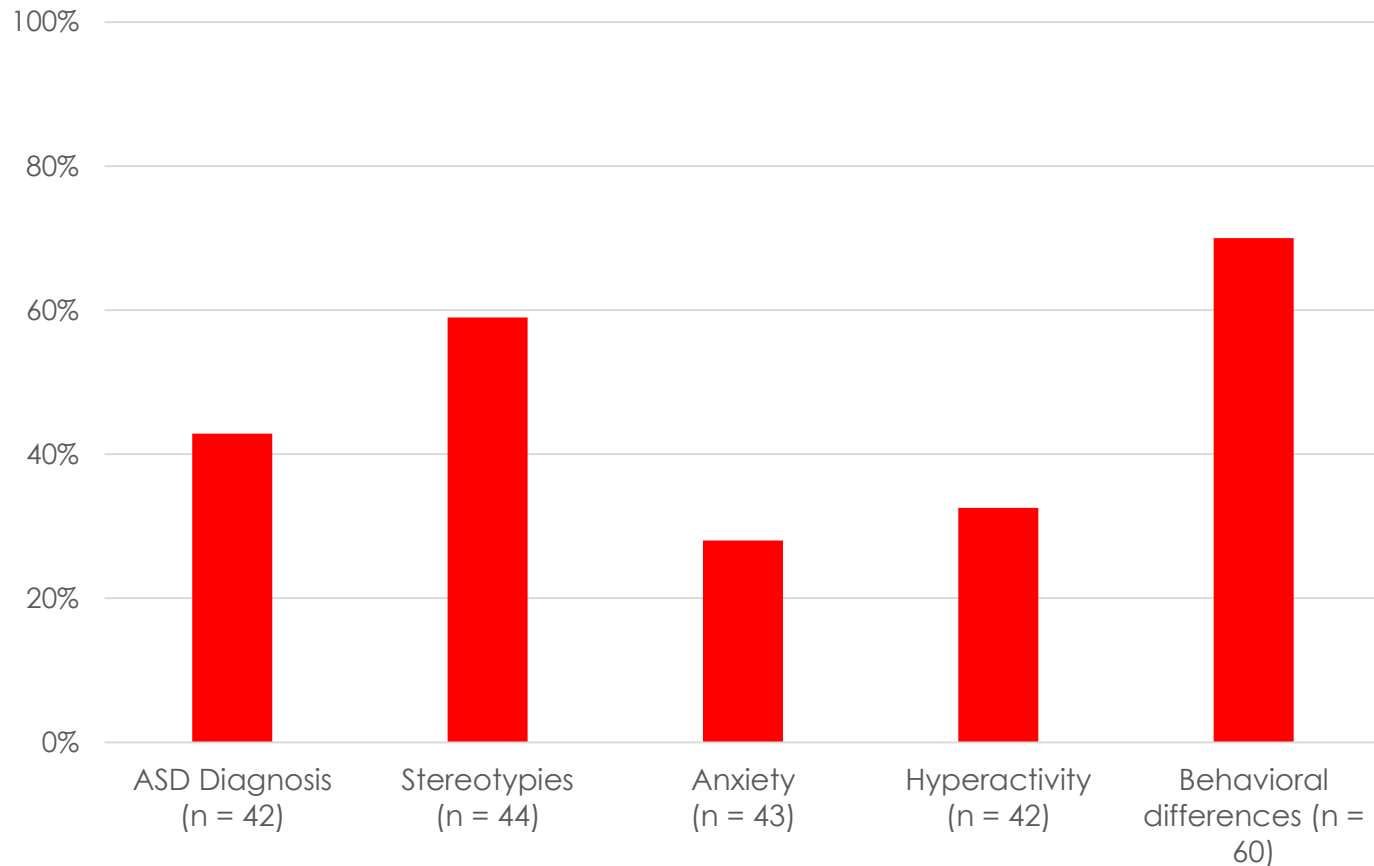
CLINICAL PRESENTATION OF *DYRK1A*

60 total, 10 participants of the TIGER study



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DISTINCT FACIAL FEATURES



c.Arg255*



p.Lys406Argfs*44



c.1098+1G>A



p.Ile48Lysfs*2



c.665-8_665-3delTCTTC



p.Asn151Lysfs*12

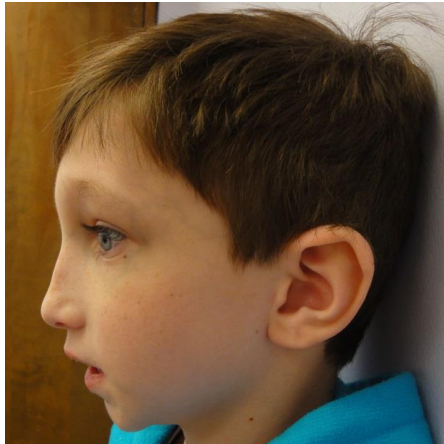


p.Ile468Aspfs*17



p.Ala498Profs*61

DISTINCT FACIAL FEATURES



p.Ala498Profs*61



p.Asn151Lysfs*12



c.665-8_665-3delTCTTTC



p.Leu295Phe



p.Ile468Aspfs*17



p.Arg255*

OTHER FEATURES



p.Ile48Lysfs*2



p.Leu295Phe



p.Ile468Aspfs*17

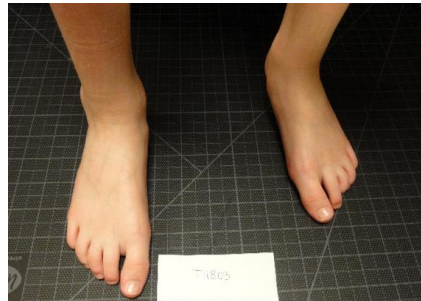


p.Arg255*

OTHER FEATURES



p.Ile48Lysfs*2



p.Ala498Profs*61



p.Asn151Lysfs*12



p.Lys416Asnfs*35



p.Ile468Aspfs*17



p.Arg255*

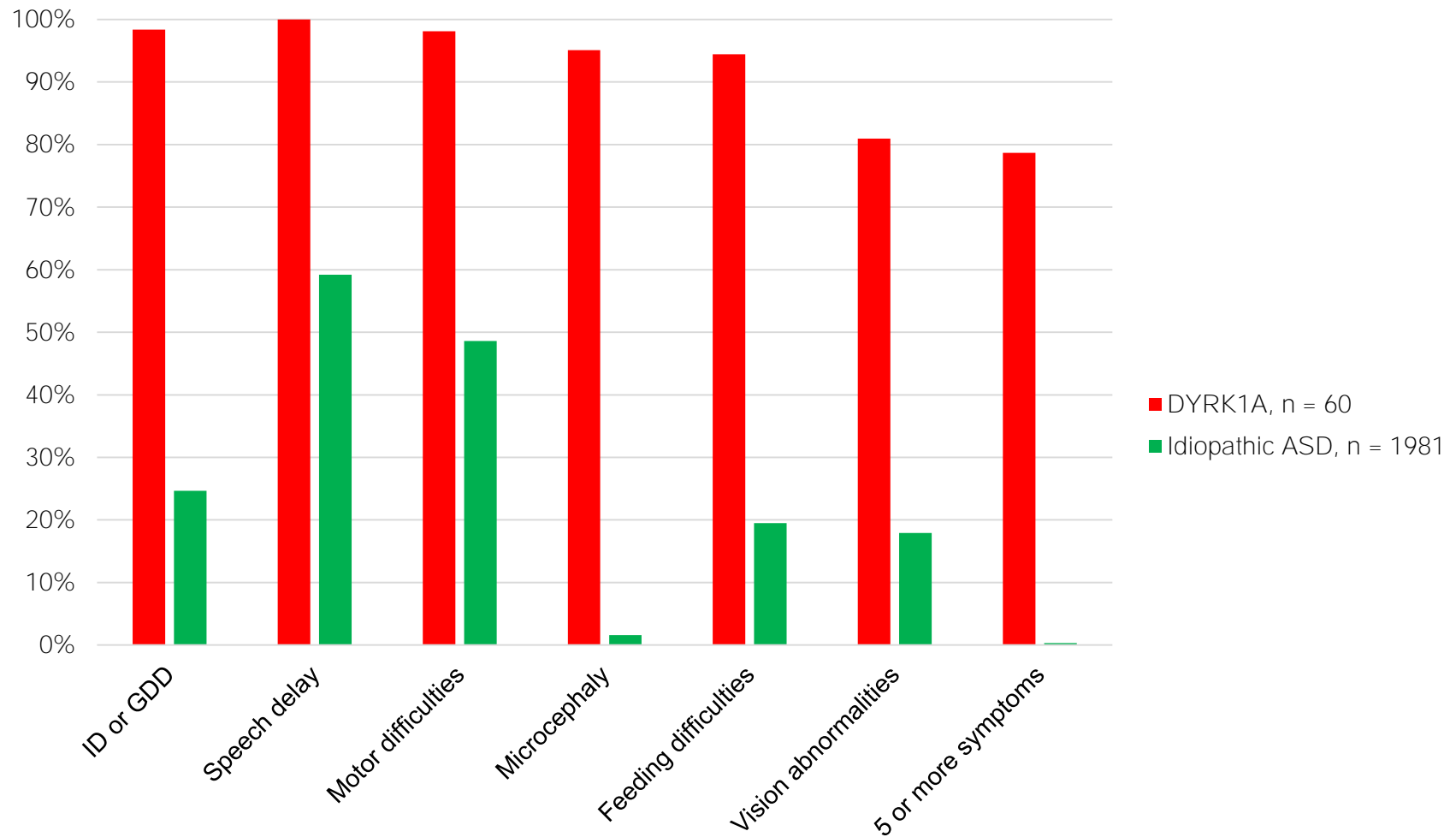


c.1098+1G>A



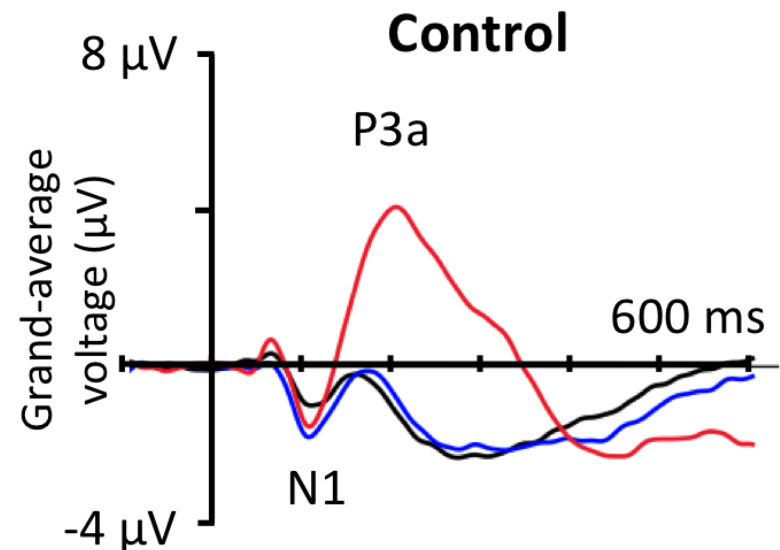
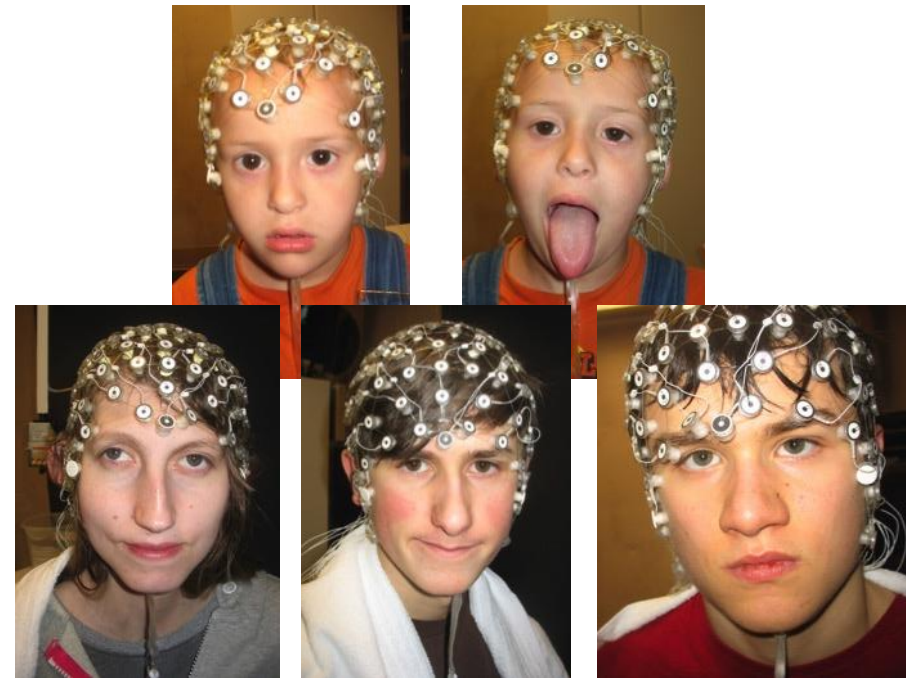
c.665-8_665-3delTCTTTC

DYRK1A CLINICAL PROFILE IS UNIQUE



DYRK1A AND THE BRAIN

- Passive auditory oddball event-related potential (ERP) paradigm
- Children watched zoo movies while hearing:
 - Frequent tones, 70%
 - Infrequent tones, 15%
 - Novel sounds, 15%
- Attention allocation → N1
 - **Infrequent** rare tone vs Frequent tone
- Attention orienting → P3a
 - **Novel** rare sound vs Frequent tone



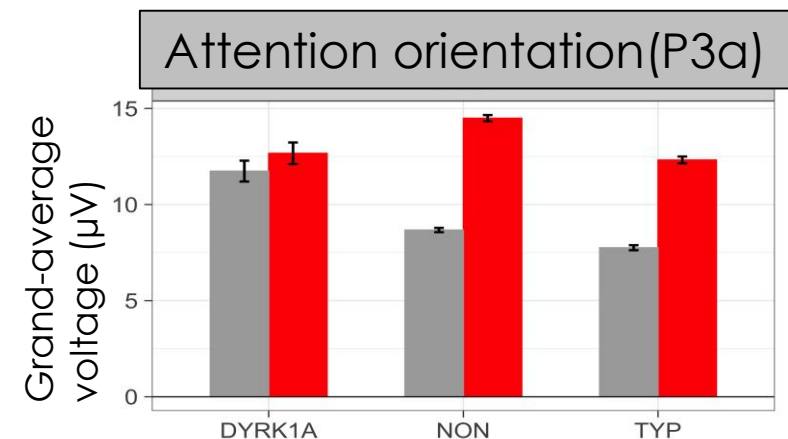
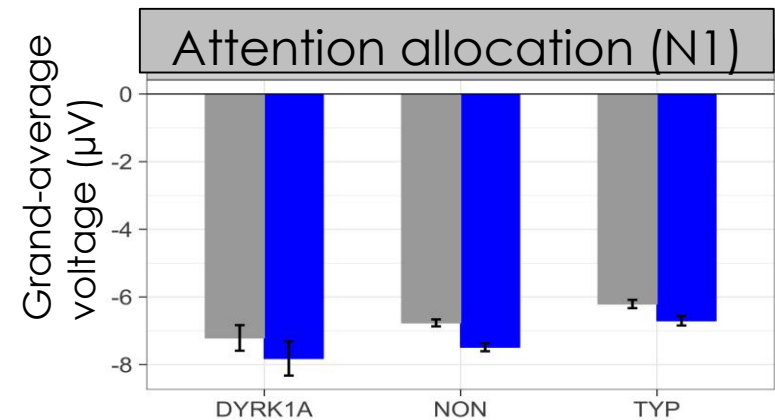
LACK OF ATTENTION ALLOCATION AND ORIENTATION IN *DYRK1A*

Preliminary data:

- *DYRK1A*, n = 9
- “Idiopathic” ASD (NON), n = 63
- Typical development (TYP), n = 33

Unlike comparison groups,
no condition differences for
DYRK1A group

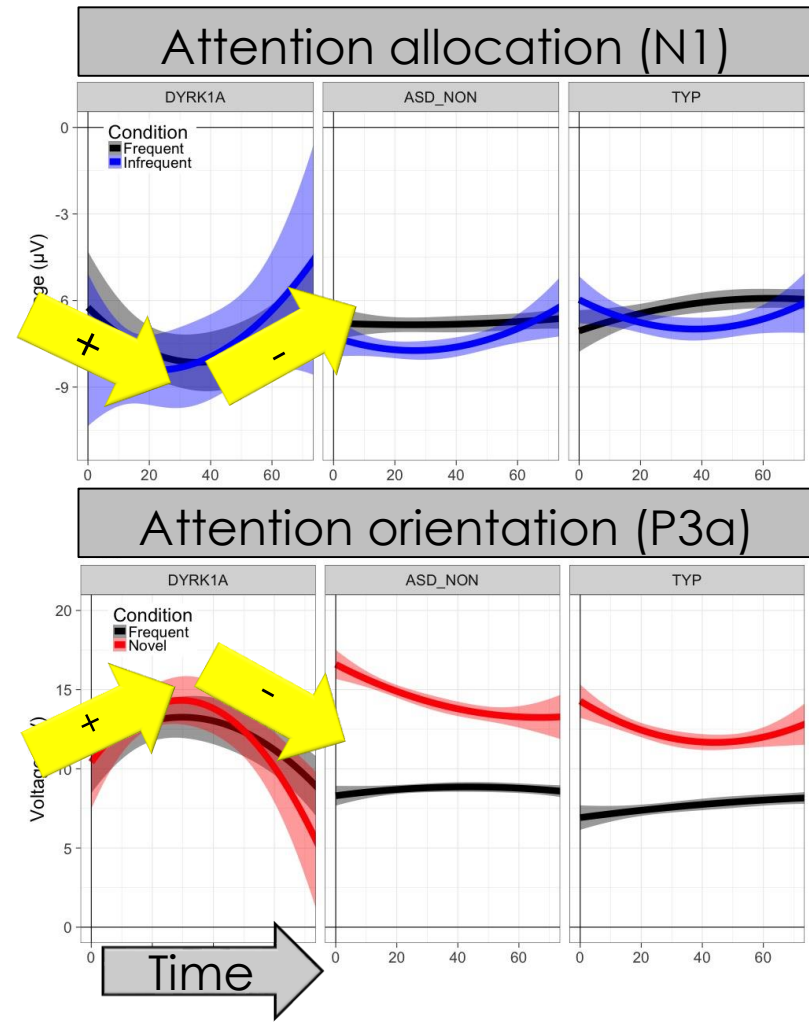
- N1: Frequent vs **Infrequent**
- P3a: Frequent vs **Novel**



HABITUATION PATTERNS ALSO ATYPICAL IN *DYRK1A*

Habituation is an index of learning – e.g., how the brain signal reduces over time.

Unlike comparison groups, *DYRK1A* group exhibited initial increase followed by a sharp reduction for all conditions.



ATYPICAL BRAIN RESPONSES INDICATE ATTENTION DISRUPTIONS UNIQUE TO *DYRK1A*

- Selective disruption to the attention system, not the auditory system
 - Possible target for intervention?
- Unique patterns of habituation may highlight a neural signature of information processing
 - Does an initial response increase indicate a critical period for learning?



IN SUMMARY

- Our understanding of the DYRK1A profile is greatly increasing – thanks to families like yours!
- Brain and eye-tracking studies have the potential to identify unique patterns to DYRK1A and its relationship to autism including cognitive and social challenges
- Important to see additional people at different ages to see what development looks like over time.

WHAT'S NEXT FOR THE TIGER STUDY?

- 1) Continue to see more families!
- 2) Collaborating functional research to understand the impact of *DYRK1A* on proteins and cell functioning
- 3) Further down the road, participation in clinical trials

WE WANT TO LEARN MORE FROM YOU!

Participate in our research!

Contact us by:

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Phone: 206-616-2889

Website: <http://depts.washington.edu/rablabs/>





THANK YOU!
QUESTIONS?