DYRK1A AND AUTISM SPECTRUM DISORDER

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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

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

Van Bon et al, 2016

Ji et al, 2015

O’Roak et al, 2012
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

Female 53%

Male 47%

AGE

Age (in years)

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
CLINICAL PRESENTATION OF DYRK1A

60 total, 10 participants of the TIGER study

- ID or GDD (n = 60)
- Speech delay (n = 60)
- Motor difficulties (n = 52)
- Microcephaly (n = 60)
- Feeding difficulties (n = 60)
- Vision abnormalities (n = 42)
- Seizures (n = 58)
- ASD Diagnosis (n = 42)
CLINICAL PRESENTATION OF DYRK1A

60 total, 10 participants of the TIGER study
DISTINCT FACIAL FEATURES

- p.Arg255*
- p.Lys406Argfs*44
- c.1098+1G>A
- p.Ile48Lysfs*2
- c.665-8_665-3delTCTTT
- p.Asn151Lysfs*12
- p.Ile468Aspfs*17
- p.Ala498Profs*61
DISTINCT FACIAL FEATURES

p.Ala498Profs*61
p.Asn151Lysfs*12
c.665-8_665-3delTCTTTTC

p.Leu295Phe
p.Ile468Aspfs*17
p.Arg255*
OTHER FEATURES

p.Ile48Lysfs*2

p.Leu295Phe

p.Ile468Aspfs*17

p.Arg255*
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 it’s 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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THANK YOU!
QUESTIONS?