An Exploration of Behavioral Phenotypes Related to *DYRK1A* and *ADNP* Gene Mutations Associated with Autism Spectrum Disorder

Christine Haensli, **Aiva Petricеks**, Eva Kurtz-Nelson, Heena Panjwani & Raphael Bernier

Bernier Lab
University of Washington

INTRODUCTION

- Autism spectrum disorder (ASD) - a complex neurodevelopmental disorder that involves challenges in speech and nonverbal communication, social interaction and repetitive behaviors
- ASD can manifest in a variety of ways hypothesized to be the result of multiple environmental and genetic factors. Two such genetic factors are disruptive mutations to genes *ADNP* and *DYRK1A*.
- Activity-dependent neuroprotective protein (*ADNP*) - a gene vital for brain formation and proper development, associated with regulation of dendritic spine formation and brain plasticity (Amram, et al., 2016; Dresner, Agam, & Gozes, 2011)
  - Mutations seen in ASD and schizophrenia (Dresner, Agam, & Gozes, 2011)
- Dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase 1 A (*DYRK1A*) - crucial for postnatal neural development, associated with dendritic growth, dendritic spine development and radial migration during cortical development (Dang, et al., 2017)
  - Mutations seen in ASD and trisomy 21 (Bon, et al., 2015)
- The aim of this project is to illuminate phenotypes associated with disruptive variations to both genes by comparing verbal, nonverbal, and adaptive skills of people with mutations to these genes to each other.

METHOD

- Participants included individuals from the TIGER study who have mutations in:
  - *ADNP* (n=9, ages 4-13 years)
  - *DYRK1A* (n=10, ages 4-24 years)
- TIGER (The Investigation of Genetic Exome Research) - explores how specific genetic events may contribute to Autism Spectrum Disorder and related developmental disorders
- Assessments administered:
  - Vineland Adaptive Behavior Scales II - assesses adaptive behavior by measuring the personal and social skills of individuals from birth through adulthood
  - Differential Ability Scales - assesses the cognitive abilities that are important to learning
    - 17 completed DAS Early Years and 11 completed DAS School Age

RESULTS

DAS

	ADNP	DYRK1A
Verbal IQ	44.615 (SD = 25.092)	47.000 (SD = 31.382)
Nonverbal IQ	41.462 (SD = 24.456)	49.133 (SD = 30.078)

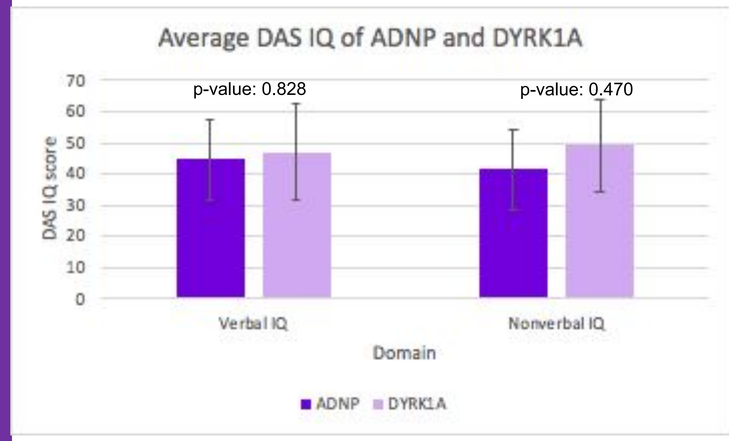
VABS II

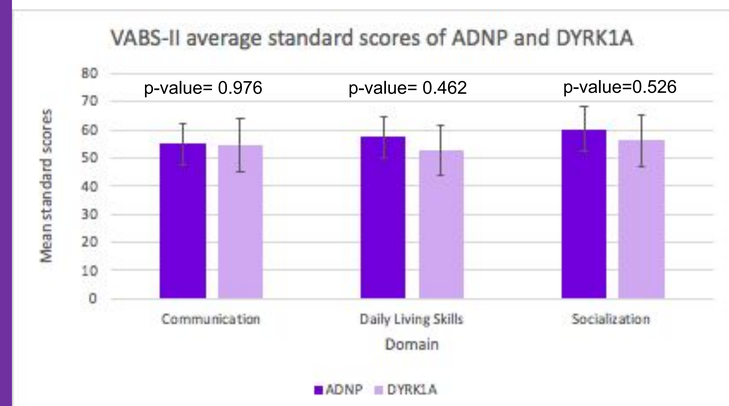
	ADNP	DYRK1A
Communication	54.923 (SD = 13.456)	54.733 (SD = 18.81)
Daily Living Skills	57.385 (SD = 13.617)	52.933 (SD = 17.351)
Socialization	60.385 (SD = 14.649)	56.333 (SD = 18.177)

Despite different molecular mechanisms, both DYRK1A and ADNP disruptive gene variant groups displayed significant adaptive and cognitive deficits.

Further research will better inform individuals and their families of the implications of living with DYRK1A and ADNP disruptive gene variant groups.

RESULTS





DISCUSSION

- Data shows no significant difference between either IQ or adaptive behaviors for participants with *ADNP* or *DYRK1A* gene mutations
- Although no differences were significant, there were some consistent trends throughout our data
  - Participants with *DYRK1A* mutations on average scored higher on verbal and non-verbal IQ tests
  - Participants with *ADNP* mutations on average scored higher on adaptive skills tests
- Although our study did not find these relationships significant, we did have a limited sample size, and these trends might be worthy of further exploration within a larger study
- One possible explanation for why there were no significant differences could be their similar mechanism of impact on dendritic spine growth, resulting in similar language, learning, and adaptive skills
- Further research on these mutations' differing phenotypes will give a better idea of the implications of living with these gene events and may inform treatment recommendations for families and individuals affected by rare mutations