Dental Manifestations in Individuals with Genetic Neurodevelopmental Disorders

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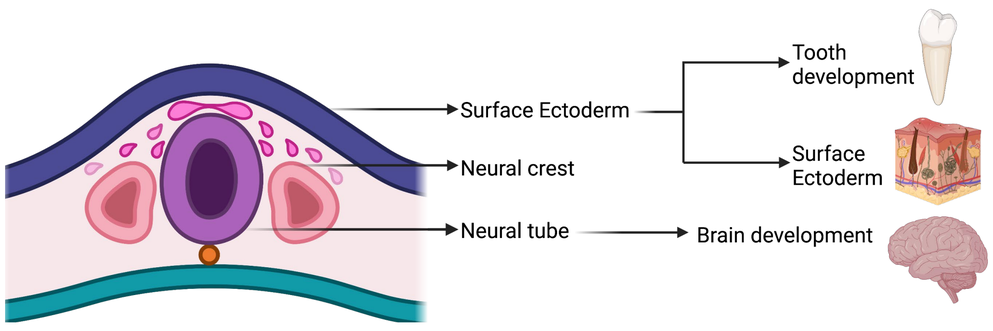
INTRODUCTION

Children with neurodevelopmental disorders often have poor oral health and dental abnormalities. An increasing number of genes have been associated with neurodevelopmental conditions affecting the oral cavity, but the specific dental features associated with many genes remain unknown.



OBJECTIVES

The goal of this study was to report the types and frequencies of dental manifestations in children with neurodevelopmental conditions of known genetic cause.

METHODS & MATERIAL

An online survey was administered through Simon's Searchlight, an international cohort of individuals with genetic neurodevelopmental disorders of known molecular cause and often associated with autism spectrum disorder.

- The questionnaire assessed ectodermal and dental features could be easily identified by caretakers.
- Responses were analyzed as a whole across all conditions and for each genetic condition separately. Frequencies were compared across conditions and with the sibling cohort which served as our control group.

SIMONS SEARCHLIGHT

RESULTS

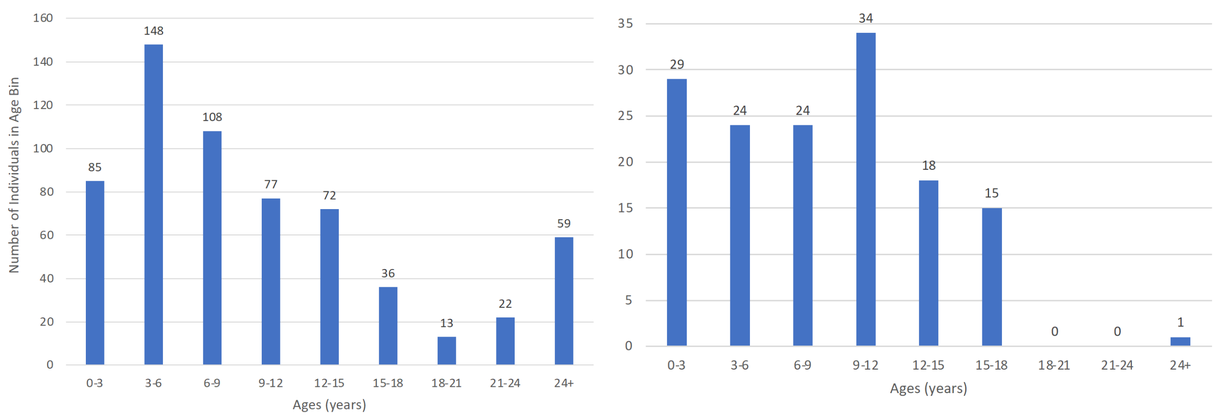
Data were collected from 620 individuals with genetic diagnoses and 145 siblings

Affected individuals

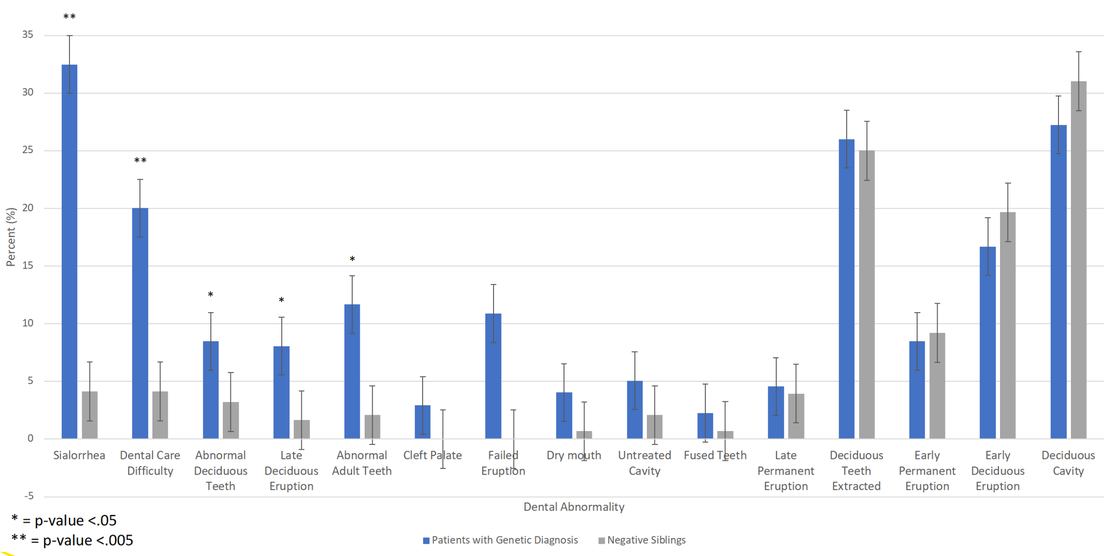
Average age: 11.4 years; standard deviation: 11.0 years

Unaffected sibling control group

Average age = 8.2 years; standard deviation of 4.7 years



Dental Abnormalities in NDD Cohort vs Unaffected Siblings



* = p-value <.05
** = p-value <.005

RESULTS

Significant Findings in Specific Conditions

Genetic condition	Description of Dental Abnormality	Frequency in Affected individuals in specified NDD	Frequency in Unaffected Sibling Control Group (All Siblings)	P-values	Risk-ratio	Frequency in Affected Individuals in Other NDDs	P-values	Risk-ratio
ADNP	Early primary tooth eruption‡	4/6 **(66.7%)**	24/122 **(19.7%)**	.02†	3.4	79/491 **(16.1%)**	.008†	4.1
CSNK2A1	Unusual primary teeth	6/14 **(42.9%)**	3/144 **(2.1%)**	.00001†	13.7	50/598 **(8.4%)**	.0008†	3.4
DYRK1A	Late primary tooth eruption§	7/13 **(53.8%)**	2/122 **(1.6%)**	<.00001†	32.8	35/484 **(7.2%)**	<.00001	7.4
PPP2R5D	High salivary flow	22/33 **(66.7%)**	6/145 **(4.1%)**	<.00001	16.1	179/568 **(31.5%)**	.00002	2.1

†Fisher's Exact Test is used when the 2x2 contingency table contains an expected frequency <5
‡Early primary tooth eruption defined as the first tooth erupting before 5 months of age
§Late primary tooth eruption defined as the first tooth erupting after 12 months of age

Deciduous Dentition Abnormalities in CSNK2A1

Participant	Sex	Age (years)	Parent description of deciduous teeth abnormality
Individual 1	M	6.4	Fused teeth
Individual 2	F	8.5	Fangs (long incisors)
Individual 3	F	13.6	Abnormal shape; all deciduous teeth had cavities before falling out
Individual 4	F	13.8	Gum was growing around the deciduous tooth and covering it, tooth disintegrating and cracking
Individual 5	M	7.8	Enamel missing, deformation of a single tooth
Individual 6	M	5.6	Small teeth; very slow to grow

DISCUSSION

The study characterized three new pathogenic gene variant/oral manifestation pairs:

CSNK2A1/abnormal deciduous teeth

- Knockout studies in animal models of pathways related to CSNKA2A1 have shown significant defects in tooth morphology.
- No malformations were recurrent in the six patients who were evaluated. Further focused evaluations may help identify specific patterns of developmental dental defects.

DYRK1A/late deciduous eruption

- May serve as a clinical marker for early referral to a pediatrician or geneticist to evaluate for this genetic condition.
- Delayed eruption is associated with a negative impact in the quality of life for a toddler, including dietary restrictions and implications for permanent dentition.

PPP2R5D/sialorrhea

- Multiple available interventions and devices for drooling can have an immediate positive impact on the quality of life for individuals diagnosed with this genetic condition.

CONCLUSION

Unmet dental care remains a significant healthcare issue for children with NDDs, which highlights the need for tailored recommendations to improve monitoring. We hope to show through this study that parent-based information is an effective way for to gather information about dental presentations for children with neurogenetic conditions and such information paves the way for personalized and improved dental care for these individuals.

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