Exploring Phenotypic and Neurocognitive Profiles in BCL11B Gene Mutations: A Case Study of a Family with Three Siblings

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Background:

BCL11B is a transcription factor gene that encodes a zinc finger domain, which is thought to play an important role in DNA binding, that is critical to the development of the nervous and immune system. Mutations in this gene are rare in the general population but associated with a range of neurodevelopmental abnormalities, intellectual disability, craniofacial dysmorphology, movement disorders, atopic disorders, and immune deficiencies. Most mutations in BCL11B arise de novo, with missense mutations often leading to the most severe neurodevelopmental defects. The findings of this poster aim to summarize current literature and to expand understanding regarding the phenotypic and neurodevelopmental abnormalities associated with mutations in the BCL11B gene.

Methods:

Literature review of previously published case reports was completed with the use of PubMed and Google Scholar. To date, 34 patient profiles were found and analyzed. An in-depth look at the phenotypic presentation of BCL11B mutations were gathered and summarized, including the known neurodevelopmental deficits seen in patients with BCL11B mutations. A paucity of information was previous published about neurocognitive functions and abilities in these individuals. We present a case series from one family with 3 full sibling cases (1 and 2: twins), who were evaluated for neurocognitive functioning across a broad battery. Testing looked at language skills, intelligence, executive functioning, learning and memory, attention, and visuospatial skills.

Results:

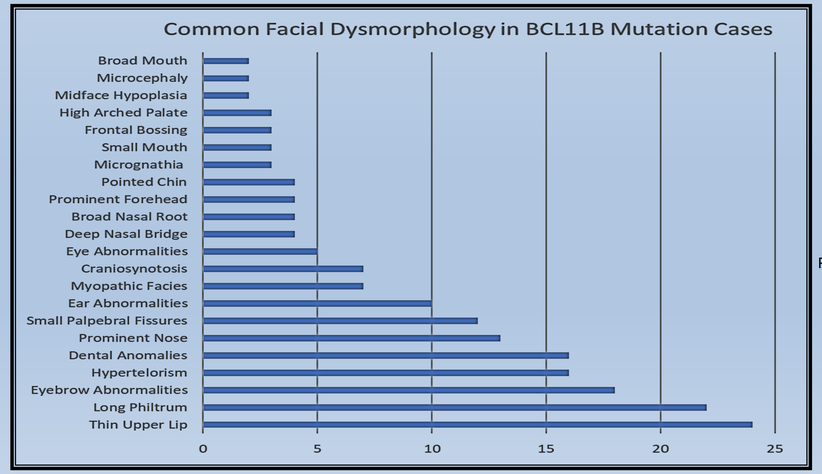

Figure 1: Looking at facial dysmorphology in BCL11B mutations.

Case 1		Case 2		Case 3	
Referred for ASD		Referred for ASD		Referred for pre-surgical evaluation	
Strengths	Weaknesses	Strengths	Weaknesses	Strengths	Weaknesses
Language skills Visual-constructional reasoning Learning and Memory Working memory Processing speed Attention Inhibition	Visual pattern detection and sequencing	Language skills Language-based learning and memory Visual learning Working memory Processing speed Inhibition	Visual memory Attention	Language skills Language-based learning and memory Visual memory Cognitive flexibility Speeded naming Inhibition Math Calculation	Verbal Fluency Visual learning Attention Processing speed Fluid reasoning Working memory Visual scanning Higher order problem solving Visual-motor integration

Table 1: Neurocognitive profile of cases based on strength and weaknesses.

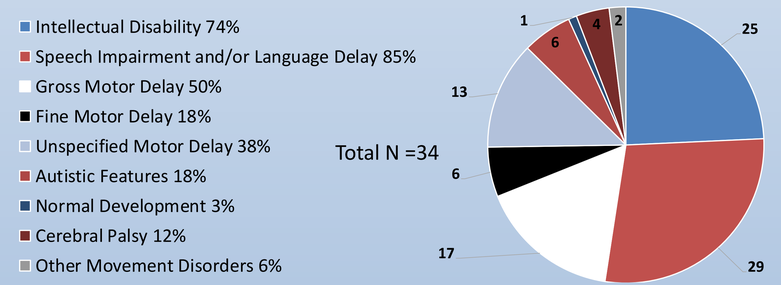

Figure 4: Developmental Features in Patients Harboring BCL11B Mutations.

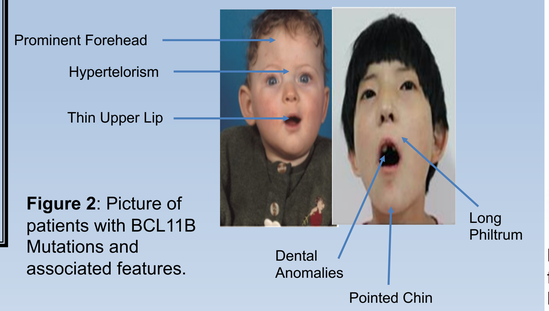

Figure 2: Picture of patients with BCL11B Mutations and associated features.

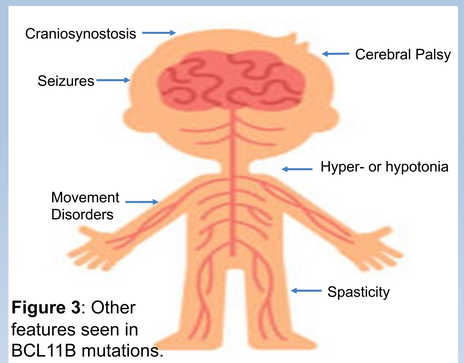

Figure 3: Other features seen in BCL11B mutations.

Discussion:

AIM 1:

- Through a review of current literature, 34 patient cases were analyzed, and developed a summary of the phenotypic and neurodevelopmental characteristics associated with BCL11B mutations.
- Most common phenotypic include: thin upper lip, long philtrum, eyebrow abnormalities, hypertelorism, and dental anomalies.
- The most common neurodevelopmental features included: intellectual disability, language and speech impairment, motor delays, and autistic features.

AIM 2:

- Case series is the first to provide data on the neurocognitive abilities of 3 full siblings with BCL11B mutations with specific cognitive deficits and functioning.
- Individuals were referred for different indications and subsequently did not all receive the same assessment measures.
- All siblings had relative strengths in language skills.
- Case 1 and 2 had strengths in executive functioning with difficulties in social communication and interaction and restricted, repetitive behaviors.
- Case 3 had strength in math calculation that was not seen in case 1 or case 2 but overall more weaknesses (e.g. deficits in visual-spatial skills, executive functioning, speeded tasks). Case 3 testing revealed weaknesses in non-dominant hemisphere functions as well as subcortical functions which were not seen in case 1 and case 2.
- None of the siblings met criteria for intellectual disability vs. literature review.

Next Steps:

Further assessment of neurocognitive profiles in individuals with BCL11B mutations with be important to gain a better understanding of the range of cognitive challenges that can be experienced. Case 3, who has the most severe deficits, is being referred for treatment with deep brain stimulation to address motor symptoms. The outcome of this procedure could have a remarkable impact on treatment and therapy options going forward for patients with BCL11B mutations.

Citations:

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