Title: *TRIO*-Related Neurodevelopmental Disorder *GeneReview* Developmental Milestones by Type of Variant

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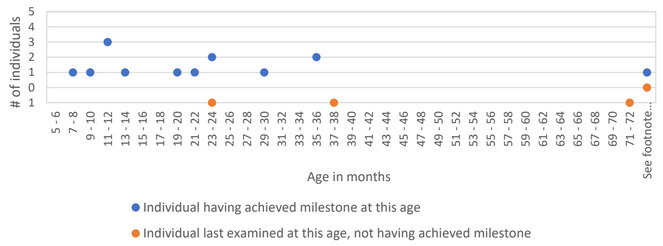
Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

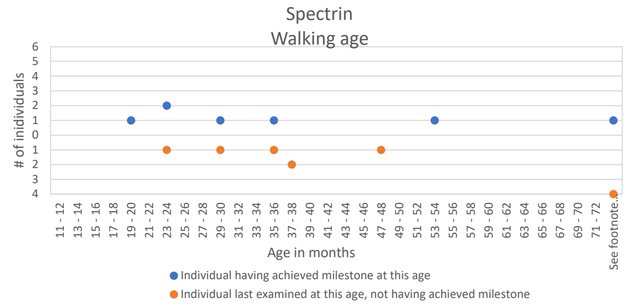
The following charts are summaries of the developmental milestones for individuals with a *TRIO* gain-of-function variant (within the TRIO spectrin domain) and individuals with a *TRIO* loss-of-function variant (within the GEFD1 domain or a truncating variant). The figure demonstrates the number of individuals having achieved the milestones of sitting, walking, and first words, with the respective age that these milestones were met (**blue dots**). As some of the individuals not having met these milestones were possibly young at the age of last assessment, for completeness, an effort has been made to also represent these individuals at the age they were last examined (**amber dots**). The last age group represents the number of individuals who either achieved the corresponding milestone after age six years (**blue dots**) or who were examined after age six years but had not achieved the relevant milestone on last assessment (**amber dots**). Additional data are provided for the subgroup of variants presumed to confer loss of function either due to a pathogenic variant within the GEFD1 domain or a truncating variant.

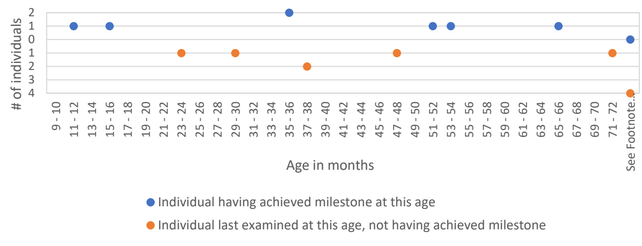
**617061**
INTELLECTUAL DEVELOPMENTAL DISORDER, AUTOSOMAL DOMINANT 44, WITH MICROCEPHALY; MRD44

**⇑ Rac1 activation**

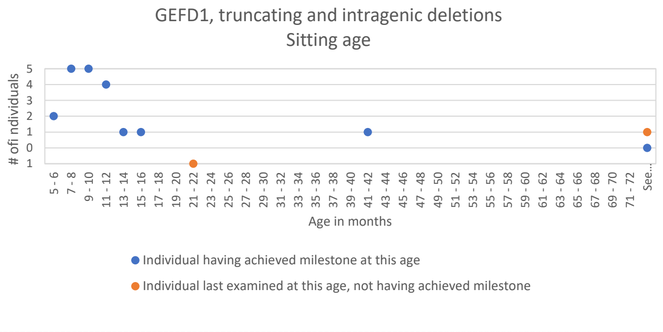
Missense variants in spectrin repeats

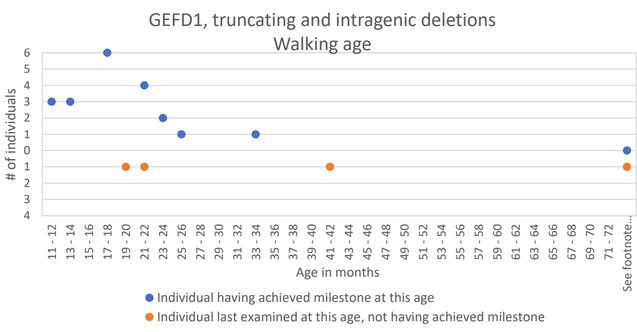


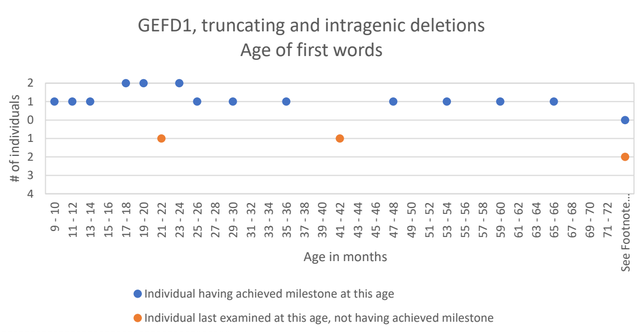



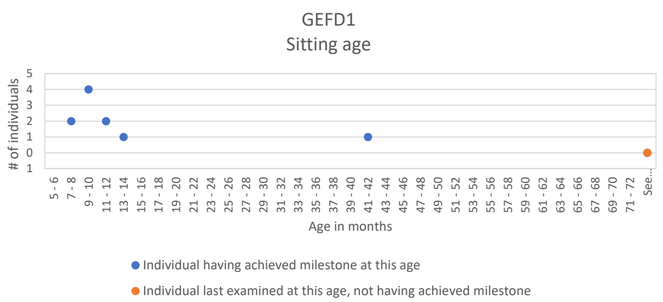

ALL VARIANTS FOR THIS PHENOTYPE CONSIDERED: Missense variants in GEFD1 domain, truncating and deletions

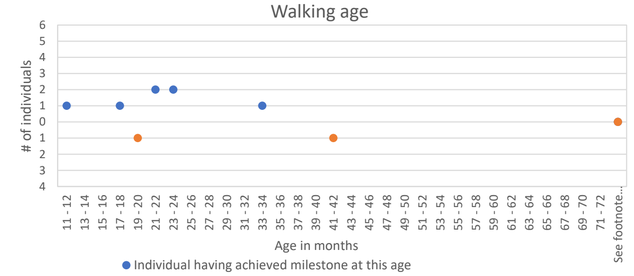


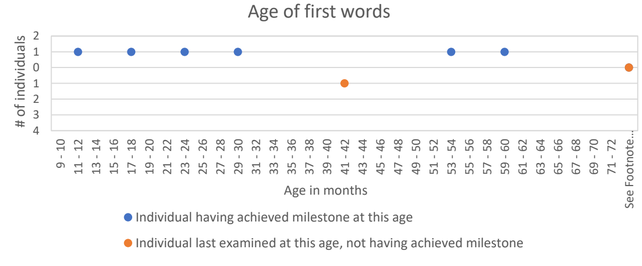



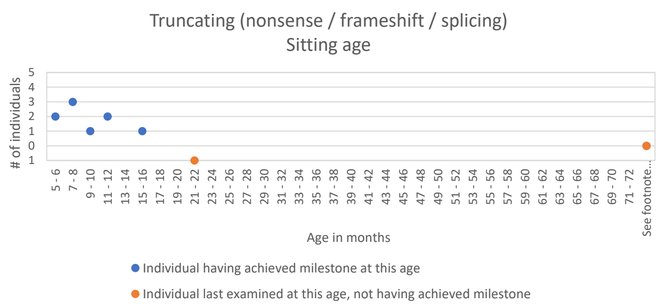

Subcategory of missense variants in GEFD1 domain only

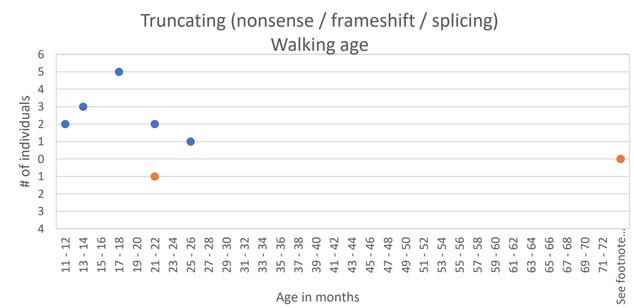


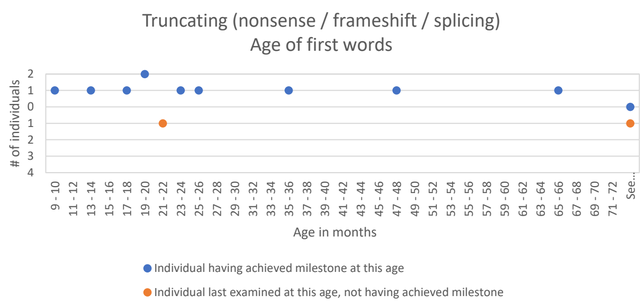




Subcategory of truncating variants only




***TRIO*-related NDD. Summary of the developmental milestones for individuals with spectrin (gain-of-function) or GEFD1/truncating (loss-of-function) variants with further details for the latter.** The figure demonstrates the number of subjects having achieved motor and speech milestones with the respective age that these milestones was met (**blue dots**). As some of the individuals not having met these milestones were possibly young at the age of last assessment, for completeness, an effort has been made to also represent those (with **amber dots**) at the age that they were last examined. The last age group represents the number of individuals who either achieved the corresponding milestone after the age of 6 years (for **blue dots**) or who were examined after the age of 6 years but had not achieved the relevant milestone on last assessment (**amber dots**). Milestones for the two principal categories of variants are presented (gain or loss of function) and the respective phenotypes (MIM #618825, Intellectual developmental disorder, autosomal dominant 63, with macrocephaly due to variants in the spectrin domain and MIM #617061, Intellectual developmental disorder, autosomal dominant 44, with microcephaly due to missense variants in the GEFD1 or truncating ones throughout the gene). Additional data are provided for the subgroup of variants presumed to confer loss of function either due to GEFD1 or a truncating variant.