KIAA2022 – further elucidating the phenotype

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Purpose

To further elucidate the phenotype associated with *KIAA2022*-mutations.

Method

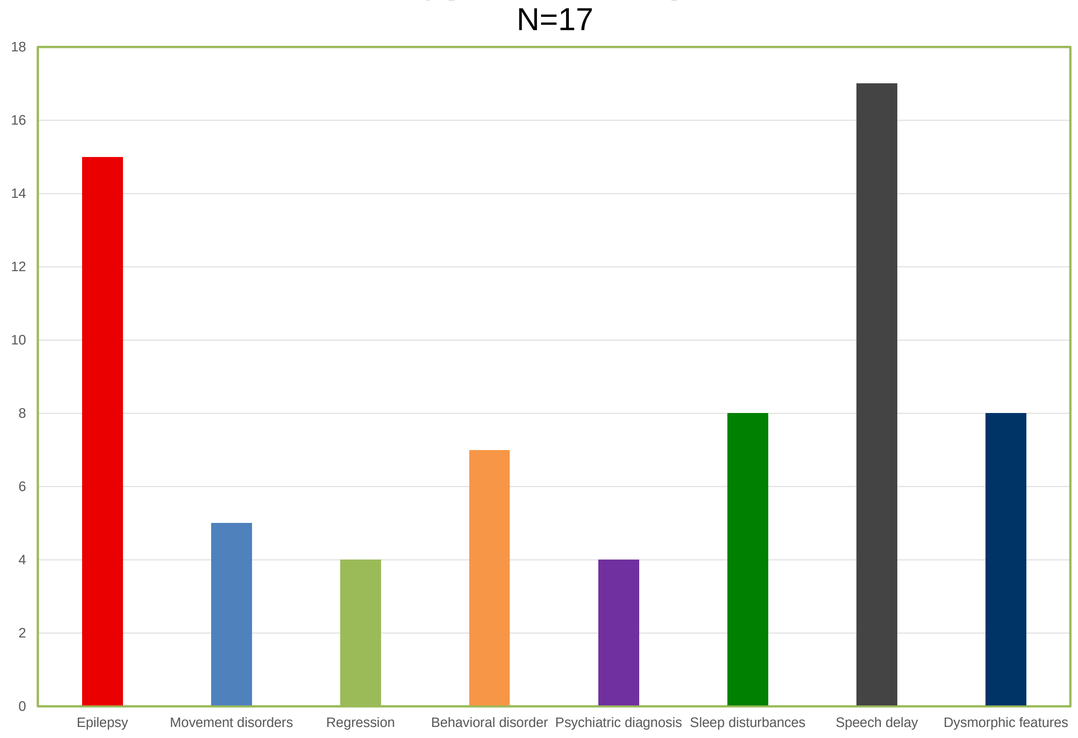
- We collected phenotypic data on 17 sporadic *KIAA2022* probands (1 male/16 females) and on a family with three affected siblings and three unaffected female carriers.
- The phenotype in previously published cases (15 males and 21 females) was reviewed in order to give a more precise description of the phenotype.

Results

- Mutations in the sporadic cases were predicted to result in a frameshift or premature stop. The mutation in the family was a probably pathogenic inframe deletion.
- All male patients had moderate to severe intellectual disability and a neuropsychiatric diagnosis. One had dysmorphic features.
- Of the 17 female patients, 5 had mild, 10 had moderate and two had severe intellectual disability. Treatment resistant seizures affected a majority of the patients (11/17). Some dysmorphic features were described in half of the female patients. Psychiatric disorders, regression and movement disorders were also described.
- No cerebral malformations were observed on MRI.
- The family consisted of three unaffected adult females and three affected siblings showing a variable phenotype: See pedigree for description.
- Comparison of the phenotype and mutation type in the new and the previously published cases showed consistency.

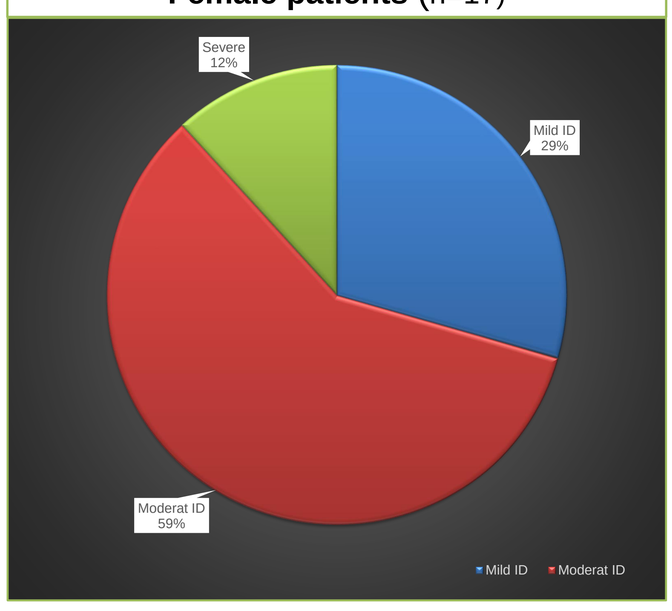
Phenotype, Female patients

N=17



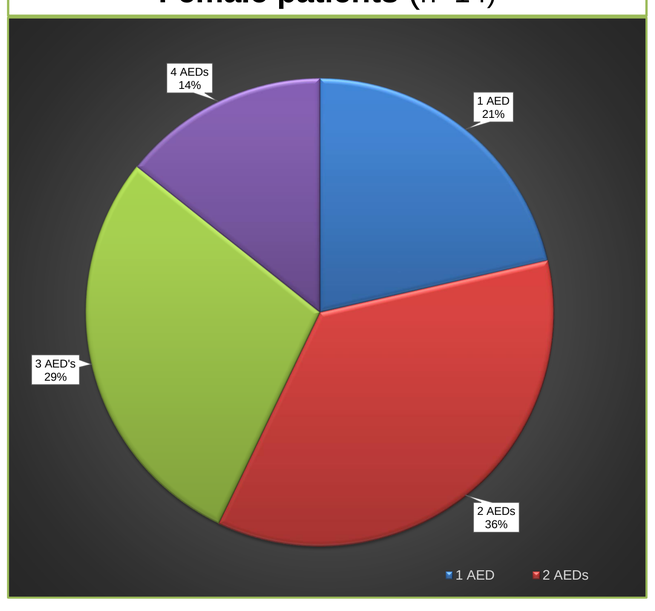
ID level

Female patients (n=17)

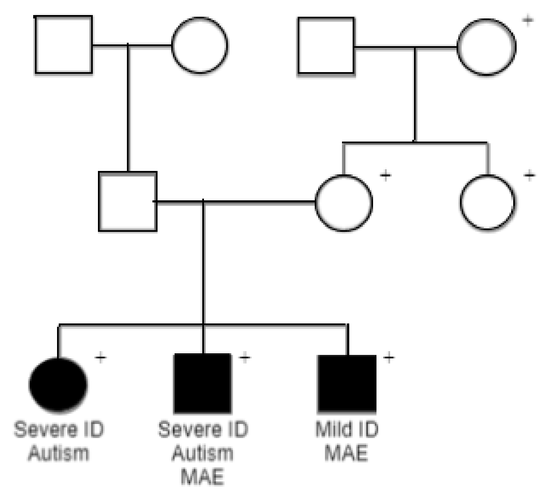


Level of polypharmacy

Female patients (n=14)



Pedigree of the family



Conclusion

- *KIAA2022* mutations are reported to cause both recessive and dominant X-linked treatment resistant seizures and intellectual disability. The phenotype presented in this study is in line with the previous reported. The phenotype in females and males overlap but females do generally show less severe intellectual disability.
- To our knowledge this is the first description of a family showing both recessive and dominant X-linked inheritance. Skewed X-inactivation could be an explanation or the phenotype in the family might not be caused by the KIAA2022 variant, since it is neither a frameshift nor a stop mutation.
- Mutation types are primarily frameshift and premature stop variants but structural chromosomal alterations affecting *KIAA2022* are also reported.

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