Neuropsychological Profile of a child with KCNQ2: Case Study

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Background

- The KCNQ2 gene mutations, a known cause of neuronal potassium channel dysfunction in brain cells, causes susceptibility to seizures beginning within the first days of life[1].
- Seizure semiology, severity and cognitive sequela can vary depending on type of KCNQ2 mutation[2,3].
- Cognitive impact ranges from moderate to severe, with no known consistent cognitive profile[4].
- KCNQ2 affects approximately 2.8 in 100,000 births: over 3,000 annual cases worldwide[5].
- **The case of an eleven-year-old girl who presented with the monoallelic mutation of the KCNQ2 gene will be examined for neuropsychological findings to highlight the presentation and cognitive profile of a KCNQ2 subtype.**

Brief History

- Medical history: multifocal seizures beginning at 2 days old and significant anxiety, both managed with medication.
- EEG indicated generalized epilepsy syndrome; right occipital focal area of dysfunction.
- History of language delay.
- Diagnosis of KCNQ2 at age 9.
- Anxiety surrounding test taking, school experiences, and seizure activity.
- **Neuropsychological evaluation conducted with a focus on processing speed, behavioral concerns, and anxiety.**

Observations

- Evaluation conducted over 3 sessions.
- Appropriate body coordination and orientation was demonstrated, though movement was somewhat slower than is typical and tasks were performed at a slower rate.

WISC-V	SS/ss
Verbal Comprehension	95 (SS)
Similarities	8
Vocabulary	10
Visual Spatial	84 (SS)
Block Design	7
Visual Puzzles	7
Fluid Reasoning	91 (SS)
Matrix Reasoning	9
Figure Weights	8
Working Memory	88 (SS)
Digit Span	9
Picture Span	7
Processing Speed	89 (SS)
Symbol Search	7
Coding	9
Full Scale IQ	89(SS)

WJ-IV Clusters	SS
Academic Skills	102
Reading	97
Mathematics	83
Written Expression	107
Broad Achievement	95

NEPSY-II Subtests	ss
Fingertip Tapping Dominant Hand Combined	3
Fingertip Tapping Non-Dominant Hand Combined	5

Tower of London	Range
Total Move Score	Impaired

Purdue Pegboard	Range
Dominant Hand	Impaired
Non-dominant Hand	Borderline/ Impaired
Both Hands	Low Average

BASC-3	Clinically Significant Levels of Anxiety and Behavioral Concern

Results

- Neuropsychological evaluation revealed low average overall cognition and average academic performances with a relative **weakness in mathematics**.
- Relative strengths of verbal comprehension, fluid reasoning, and written expression were identified.
- Cognitive processing speed was variable **with impaired fine motor speed** (right weaker than left) and **generally slow movement** (as noted throughout the evaluations), while performance on several time-limited measures was adequate. Overall **motor movements were slow**, yet she was able to increase her speed for short bursts of time (on SS and CD).
- Behavior assessments supported **anxiety** and **emotion regulation weakness**.

Conclusions

- This eleven-year-old girl with a rare KCNQ2 gene mutation demonstrated a more preserved than previously documented cognitive and behavioral profile, contributing to our limited knowledge of how KCNQ2 presents.
- **Impairment in motor speed** and **weaknesses in mathematical learning** were evidenced**. Anxiety** and **emotional reactivity** were evidenced as well. **Processing speed** was generally **slow** across domains with the notable **exception** of the WISC-V Coding.

Diagnoses made:

- **Specific Learning Disorde**r with Impairment in **Mathematics** (DSM-5: 315.1)
- **Generalized Anxiety Disorder** (DSM-5: 300.02)
- **Emotional Reactivity**

References

1. Singh, N. A., Charlier, C., Stauffer, D., DuPont, B. R., Leach, R. J., Melis, R., ... & Leppert, M. (1998). A novel potassium channel gene, KCNQ2, is mutated in an inherited epilepsy of newborns. *Nature genetics*, *18*(1), 25-29..
2. Neubauer, B. A., Waldegger, S., Heinzinger, J., Hahn, A., Kurlemann, G., Fiedler, B., ... & Sander, T. (2008). KCNQ2 and KCNQ3 mutations contribute to different idiopathic epilepsy syndromes. *Neurology*, *71*(3), 177-183.
3. Millichap, J. J., Park, K. L., Tsuchida, T., Ben-Zeev, B., Carmant, L., Flamini, R., ... & Cooper, E. C. (2016). KCNQ2 encephalopathy: Features, mutational hot spots, and ezogabine treatment of 11 patients. *Neurology Genetics*, *2*(5).
4. Malerba, F., Alberini, G., Balagura, G., Marchese, F., Amadori, E., Riva, A., ... & Striano, P. (2020). Genotype-phenotype correlations in patients with de novo KCNQ2 pathogenic variants. *Neurology Genetics*, *6*(6).
5. *What is KCNQ2 epilepsy*. KCNQ2 Cure Alliance. (2020, January 23). Retrieved September 10, 2022, from https://www.kcnq2cure.org/kcnq2-epilepsy/