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Analysis of treatments used for individuals with Rett Syndrome who experience seizures

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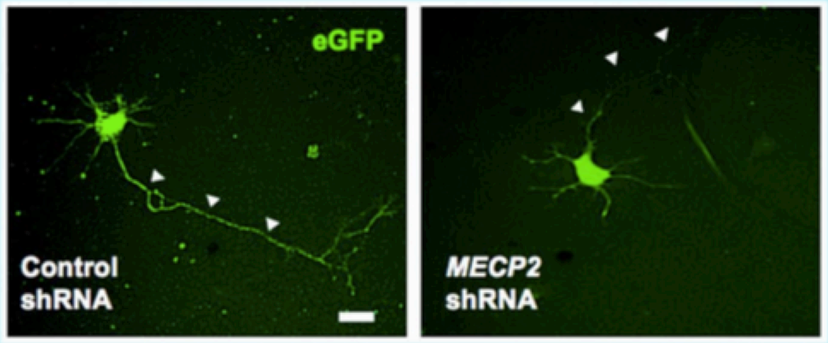
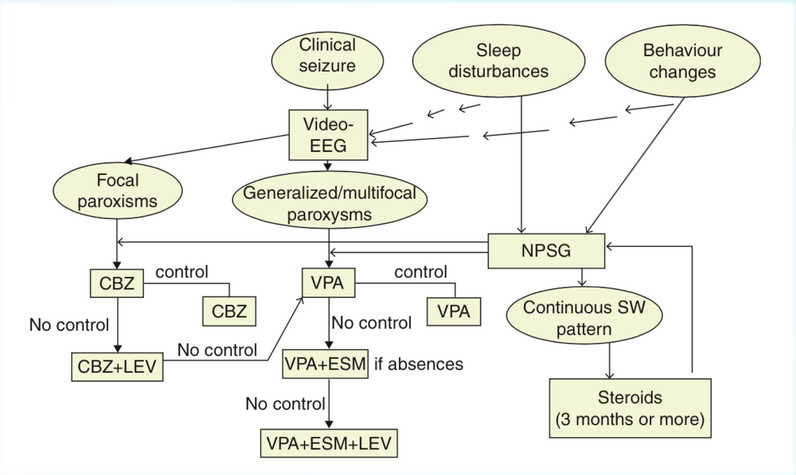
Rett Syndrome

Rett Syndrome (RTT) is a neurodevelopmental disorder solely affecting females, and is caused by genetic mutations in the methyl CpG binding protein 2 (MeCP2) gene. The MeCP2 gene produces the MeCP2 protein, which has many diverse functions including regulating the brain-derived neurotrophic factor (BDNF) gene, which produces the BDNF protein. Individuals with RTT have mutated MeCP2 genes, which results in low levels of MeCP2 protein and BNDF protein.

Regardless of these genetic mutations, individuals with RTT develop normally until about six to eight months of age. After this developmental window, neurological differences become present which are followed by phenotypic differences during which motor skills, language skills and social skills are impaired. In addition to these impairments, individuals with RTT also experience other symptoms such as breathing problems, sleep apnea and seizures. Seizures are a common symptom associated with RTT, as up to eighty percent of individuals with RTT experience seizures.



Medication(s)	Cases on this medication/ combination	Median age	Monthly seizure rate			
			P_{10}	P_{50}	P_{90}	Mean (95% CI)
Carbamazepine	19	15.5	0.0	0.6	15.3	3.4 (3.1–3.6)
Sodium valproate+lamotrigine	17	13.8	0.1	3.8	30.3	26.2 (25.5–29.6)
Sodium valproate	16	10.5	0.0	0.2	13.7	3.4 (3.1–3.7)
Carbamazepine+sodium valproate	6	16.5	0.0	1.0	2.8	1.2 (0.9–2.0)
Lamotrigine	5	9.7	0.0	2.8	24.8	7.6 (6.9–8.3)
Carbamazepine+lamotrigine	5	14.1	0.5	5.4	30.3	9.0 (8.2–9.3)



Conclusion

The use of AEDs is very common for females with RTT who experience seizures. However, due to the number of side effects associated with AEDs, they are not readily available or desirable for all females with RTT. Focusing research on treatments that will halt or prevent the seizures from occurring rather than treating the seizures as they appear will prove to be more beneficial. Two such treatments in consideration are increasing the amount of the BDNF protein as well as increasing the MeCP2 protein present in the brain. Previous research in mice has shown that increasing the levels of these two proteins alleviates RTT-like symptoms. However, additional research must be done in order to implement these treatments effectively on a widespread scale. These treatments also have the potential to be administered during the developmental window in which neurological changes are present but phenotypic changes associated with RTT are not. Treating females with RTT who also experience seizures during this developmental window can potentially halt symptoms from appearing or help curb symptoms at an earlier stage in the lives of these individuals.

Epileptic Seizures

Seizures are of a major concern for individuals with RTT because they are fairly common and make life much more difficult for these females. A female with RTT has a 5-38% chance of developing epilepsy and experiencing seizures as opposed to a 1-2% chance in regular individuals. Some individuals experience seizures in childhood, some in puberty and some others well into adulthood. Thus seizures can occur at any age, but the frequency of seizures has been found to decrease significantly after the age of twenty.

Currently, the most commonly used medication is anti-epileptic drugs (AEDs). For individuals who have milder seizures, only one AED is prescribed. In other words a monotherapy strategy is used. For individuals who have other complications or more severe forms of seizures, a polytherapy approach is used where two or more AEDs are used in combination. AEDs, however, come with many side effects. For example, AEDs used in monotherapy or polytherapy can reduce vitamin D levels thereby increasing that individual's risk for fractures.

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