

DO MANY PRESUMED CRYPTOGENIC EPILEPSIES EVENTUALLY TURN OUT TO BE IMMUNE-MEDIATED? - NO

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The term "cryptogenic epilepsy" was introduced in the 1989 revision of the ILAE classification, defined as a focal or generalized seizure disorder that is considered likely symptomatic but where, in the individual patient, the etiology cannot be sufficiently identified. An authoritative 1997 review concluded that in the majority of cases (55-89%) the cause remained unidentified. In the 2010 revised classification this term was abandoned, but was actually replaced by epilepsy of "unknown" etiology.

Modern era imaging with continuously improving MRI technology has revolutionized the ability to identify epileptogenic brain lesions. A whole host of pathologies (such as small focal cortical dysplasias) has become apparent and diagnosable. This has led to a definite structural etiology in many formerly "cryptogenic" cases.

Spectacular advances in molecular genetics have elucidated a rapidly growing host of new genes and mutations, which has led to a definite genetic etiology in many other formerly "cryptogenic" cases.

Various CNS insults, including trauma, stroke, infection and perinatal injury, can induce inflammation in the brain. The inflammatory response plays an important role in epileptogenesis, and once seizures develop they can contribute to perpetuate inflammation in the brain. However, this important pathophysiological concept does not mean that the etiology of epilepsy and its classification in these cases has changed: In the past they were classified as symptomatic epilepsy due to trauma, stroke, infection or perinatal injury, and the same classification is valid today.

Previously "cryptogenic" epilepsies which have eventually turned out to be immune mediated are quite rare. The most frequently observed autoimmune epilepsies have been associated with anti-VGKC-complex (mainly anti-LGI1) and the anti-NMDA receptor. Even these two entities are rare, and have distinct clinical presentations which certainly account for only a small minority of "cryptogenic" cases.

In conclusion, many previously "cryptogenic" epilepsies eventually turn out to be of genetic or structural origin, but true autoimmune epilepsies are still rare.