

THE ROAD TO INTRACTABILITY

How Long Does It Take for Partial Epilepsy to Become Intractable?

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PURPOSE: Much remains unknown about the natural history of intractable localization-related epilepsy, including how long it typically takes before intractability becomes evident. This information could guide the design of future studies, resolve certain discrepancies in the literature, and provide more accurate information about long-term prognosis.

METHODS: Individuals evaluated for resective surgery for refractory localization-related epilepsy were prospectively identified at the time of initial surgical evaluation at seven surgical centers (between 1996 and 2001). The latency time between onset of epilepsy and failure of second medication and history of remission (≥ 1 year seizure free) before surgical evaluation were examined with respect to age at onset, hippocampal atrophy, febrile seizures, and surgical site.

RESULTS: In the 333 patients included in the analysis, latency time was 9.1 years (range, 0–48), and 26% reported a prior remission before surgery. A prior remission of ≥ 5 years was reported by 8.5% of study participants. Younger age at onset was strongly associated with longer latency time ($P < 0.0001$) and higher probability of past remission ($P < 0.0001$). In multivariable analyses, age at onset remained the most important explanatory variable of both latency time and prior remission.

CONCLUSIONS: A substantial proportion of localization-related epilepsy may not become clearly intractable for many years after onset. This is especially true of epilepsy of childhood and early adolescent onset. If prospective studies confirm these findings and the underlying mechanisms behind these associations become understood, this raises the possibility of considering interventions that might interrupt such a process and some day prevent some forms of epilepsy from becoming intractable.

COMMENTARY

Because resective brain surgery is often successful in ameliorating epilepsy that is resistant to control with pharmacotherapy, accurate and early identification of patients who are destined for intractability is vital. As the authors of the present study point out, many questions remain unanswered concerning the natural history of intractable localization-related epilepsy. In this article, Berg et al. focus on ascertaining the latency between the onset of epilepsy and the point at which the disorder has declared itself to be intractable, as well as the factors that influence this timeline. This report analyzes data obtained from an ongoing prospective study assessing the outcomes of the surgical treatment of epilepsy.

Sufficient information for 282 of 333 patients was available from medical records and structured interviews with patients to assess the time to intractability—defined in this study as the time between the occurrence of the second unprovoked seizure and failure of the second antiepileptic medication (AED). This latency time averaged 9.1 years but demonstrated an enormous range from 0 to 46 years. In multiple linear regression analysis that evaluated the presence of febrile seizures, hippocampal atrophy on magnetic resonance imaging (MRI), and type of surgery undertaken (temporal vs. extratemporal resection), age at onset was independently and significantly associated with the latency time, with younger onset age associated with a longer lag time to intractability. Additionally, more than a fourth of the patients had experienced a remission period of a year or longer, some (6.7% of the entire group) with multiple periods of remission and a number (8.5%) with protracted seizure-free periods of ≥ 5 years. This report thus helps to define the natural history of localization-related epilepsy in patients ultimately presenting for surgical treatment, highlighting the fact that intractability may not be evident in some patients for years after their epilepsy-defining diagnosis.

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