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In the current issue of *Epilepsia*, Fisher and colleagues provide a number of recommendations for practical operational definitions for epilepsy.[1] The recommendations address three areas.

1. A Recommendation that Epilepsy is a Disease
   They recommend that epilepsy be considered a disease rather than a disorder. They define a disease as a condition in which there is generally a lasting (or permanent) derangement of normal function, whereas a disorder represents a functional disturbance (for example, a seizure), not necessarily permanent.
2. An Operational Definition of Epilepsy
   The authors provide recommendations for three practical operational definitions of epilepsy that are equivalent and that they feel bring the term epilepsy into better agreement with current "common use."

The first operational definition is the same as the definition recommended by the International League Against Epilepsy (ILAE) Commission on Epidemiology: two or more unprovoked seizures occurring >24 h apart.[2,3] This recommendation was based on data demonstrating that the summary risk for an additional unprovoked seizure following a first unprovoked seizure is in the range of 40%, whereas the summary risk for further unprovoked seizures approaches 80% in those who have experienced two (or more) unprovoked seizures.[4]

The second definition is probabilistic. A person with a single unprovoked seizure and with a risk of approximately 60% or more of having a second seizure in the next 10 years would be considered to have epilepsy. The authors appropriately recommend that people with reflex seizures be considered to have epilepsy.

The third definition relates to epilepsy syndromes. Epilepsy may be diagnosed even in the absence of behavioral seizures if an epilepsy syndrome can be diagnosed (an example provided was the Landau-Kleffner syndrome).

3. A Recommendation as to When Epilepsy is "Resolved"
   Resolution of epilepsy, a term implying that a person no longer has epilepsy, was recommended to be present when an individual has been free of seizures for at least 10 years and has not taken antiseizure medication for 5 years.

Positive Factors in the Definitions

The definitions represent an attempt to provide epileptologists and other health care providers with operational definitions of what epilepsy is, when epilepsy is present even in the absence of recurrent unprovoked seizures, and when epilepsy can be considered no longer present. It is an attempt to integrate current clinical information to refine the definition of epilepsy. For this the authors are to be congratulated. Their hope was that these definitions will allow for earlier detection of people at risk for epilepsy leading to earlier interventions and presumably better outcomes.

Potential Problems with Definitions

The first definition is data driven. Given the percentages included in the second definition, it seems to be a data driven systematic assessment. On closer examination, however, the second definition represents an expert consensus and has limited substantive data to support the recommendations.

Recurrence Risk Following a First Seizure and Equivalency to Epilepsy Defined as Two Unprovoked Seizures (Definition 2)

It does seem reasonable to declare epilepsy to exist when estimated seizure recurrence is equal to or exceeds that of the risk following a second unprovoked seizure. It is not clear how the estimate of "about" 60% recurrence risk within

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10 years of a first unprovoked seizure was derived. In the Multicentre Trial for Early Epilepsy and Single Seizures (MESS) study, people with more than one seizure at enrollment who were assigned to a delayed treatment arm had a recurrence risk of 60% at 2 years.[5] In the study by Hauser and Colleagues, recurrence risk following two seizures was also 60% at 2 years following the second seizure (similar to the MESS study), and was 73% by 5 years following the second seizure.[4] In the study of Hauser and colleagues, there were no reliable data available beyond 8 years after the second seizure. It seems that there are no published data to estimate the recurrence risk following a second seizure by 10 years, but the 60% risk level suggested in the definition underestimates a data-driven recurrence risk by at least 25%.

Situations Analyzed as Potential Epilepsy after a Single Unprovoked Seizure

Acute Symptomatic Seizure

The authors outline data demonstrating that people with only acute symptomatic seizures including complex febrile seizures or febrile status epilepticus have a risk of <60% for subsequent unprovoked seizures and should not be considered epilepsy.[6–8]

Unprovoked seizure in the context of a structural lesion

Data do support a sufficiently high recurrence risk in some stroke patients to consider a first unprovoked seizure to be epilepsy. The authors provide scenarios for various situations for which a diagnosis of epilepsy might be considered. The authors example of a seizure following a cerebrovascular insult (example 2 in the authors manuscript) falls into this category. Stroke (as epilepsy) is a heterogeneous condition that varies according to mechanism, anatomic region, and size.[9] Although this risk estimate is sufficiently high in this individual with a large middle cerebral infarction, the same is probably not true for an individual with a brainstem infarction or in the 25% of the population older than 80 with an asymptomatic vascular lesion identified on imaging.[10] The authors suggest that people with brain trauma or with central nervous system infection also meet these criteria, but no data are presented on these conditions. A more detailed assessment of absolute and differential risks for a second seizure in each condition based on specific clinical features and corresponding estimates of seizure recurrence would have been useful. This could highlight the group for which the term epilepsy would be appropriate.

Epilepsy in Syndromes without Seizures

It seems reasonable to consider children with Landau-Kleffner syndrome to have epilepsy even without clinical seizures, but some discussion might have been appropriate. The child with a centrotemporal spike representing a horizontal dipole (the electroencephalography [EEG] benign signature of rolandic epilepsy of childhood) or the child with a 3 s run of a generalized spike and wave discharge on EEG who never had a clinical seizure could also potentially meet the definition of epilepsy. The distinction among these three examples in relation to a diagnosis of epilepsy may be one of quantity of epileptiform activity.

People with Resolved Epilepsy

The definition of "resolved epilepsy" again seems to be based on "expert opinion" and seems arbitrary. A person who is seizure free for >10 years and off medications for 5 years still has an annual seizure recurrence risk of 0.5% and 1%.[11–13] This can be translated to a 10–20-fold increase in risk for an unprovoked seizure when compared to the general population. It would seem that the level of residual risk for further seizures would be a better starting point for this definition (annual risk of 1% for example). This allows for individualized determination of the time at which this definition is met, factoring in variables such as age, seizure type, and persistence or resolution of EEG abnormalities.

Implications of These Operational Definitions

Need for specificity in any clinical publication or research activity

One result of the use of these definitions will be the need to specify the definitions of epilepsy used in any clinical study. If multiple investigators are involved in a report, investigator-specific definitions may be necessary.

Need for education

Clinicians involved in the care of newly diagnosed people with epilepsy need to be informed not only of the recommendations, but also provided an assessment of the risks for seizure recurrence in different clinical situations. To this end, guidelines should be established when data are sufficient to provide an estimate of risk, and areas where information is deficient should be highlighted. The authors clearly state that in the absence of information regarding recurrence, the default definition should be recurrent unprovoked seizures. I suspect that many clinicians will be too quick to use the term epilepsy despite absence of data.

Need for further research

Regardless of the level of risk used to define epilepsy following a first unprovoked seizure, there is a need to clarify the actual level of risk in various clinical situations and risk

modification by factors such as age, mechanism of insult, and severity of insult. There are limited data available for most conditions at this time.

Summary

The report by Fisher and colleagues is an excellent first step to provide operational definitions of epilepsy but there is considerably more to be accomplished. In the past absence of data expert opinion had a place in establishing definitions. When data is available, evidence based systematic review seems more appropriate[14]. Definition 1 is evidence based. For epilepsy definition 2, systematic reviews could be undertaken to provide definitive risk estimates to define epilepsy in association with putative clinical scenarios using as a baseline risk for further seizures in those with two unprovoked seizures and identify areas where further work is necessary. To define "resolved epilepsy," a level of risk should be set (for example 1% per year) rather than using an arbitrary time of seizure freedom. A systematic assessment of data could then be undertaken to determine when this risk is attained. In successful surgical cases for example, the point at which seizure recurrence risk reaches 1% may be less than a 10 years of seizure freedom. It remains to be seen how the proposed definitions will influence the clinical course of epilepsy. Let's hope that these modified definitions lead to both improved patient function and outcomes and act as a stimulus to further clinical research.

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