The Comorbidities of Epilepsy: Introduction

Marco Mula, MD, PhD, FRCP, FEAN, is Editor of ACNR's Epilepsy Series. He is Consultant Epileptologist at St George's University Hospitals NHS Foundation Trust, and Reader in Neurology at St George's University of London, UK. He is currently Editor-in-Chief of Epilepsy & Behavior, a member of the Editorial Board of many journals in neurology and psychiatry including Epilepsia Open, the Journal of Epileptology and the British Journal of Psychiatry. He has a special interest in all clinical aspects of epilepsy with special reference to the cognitive and psychiatric effects of antiepileptic drugs.

Correspondence to: Marco Mula, MD, PhD, FRCP, FEAN, Epilepsy Group, Atkinson Morley Regional Neuroscience Centre, St George's University Hospitals NHS Foundation Trust, Blackshaw Road, London SW17 0QT, UK.

E: mmula@sgul.ac.uk

Epilepsy is one of the most frequent neurological disorders after stroke and headache, affecting over 70 million people worldwide, and it is now widely accepted that having epilepsy does not simply mean having recurrent seizures. In fact, epilepsy rarely stands alone and more than 50% of patients with epilepsy have one or several additional medical problems [1]. This is reflected in the new multiaxial classification of the epilepsies of the International League Against Epilepsy that includes comorbidities along with seizure types, aetiologies and syndromic classification [2].

The word "comorbidity" dates back to Alvan Feinstein who introduced this term in 1970 referring to any distinct additional clinical entity that existed during the clinical course of a patient's index disease [3]. However, in the context of epilepsy, the term "comorbidity" includes a heterogenous group of conditions whose pathophysiology can be quite different [4]. Some conditions may coexist simply because one is the cause of the epilepsy like, for example, stroke and epilepsy or neurocisticercosis and epilepsy. In other cases, the condition is the consequence of having epilepsy or its treatment like for example osteoporosis and epilepsy or sexual dysfunction and epilepsy. Still, some conditions may share with epilepsy a common aetiology, like autism and epilepsy in the context of Tuberous Sclerosis Complex, or may be linked by a more complex bidirectional relationship like epilepsy and depression.

Whether these problems are due to shared biological mechanisms, a consequence of having epilepsy or simply due to the unfortunate occurrence of two conditions in the same individual, there is no doubt that the management of these patients can be challenging [4]. This can be due to the potential for drug-drug interactions that Neurologists need to be aware of or because the comorbid disorder has an impact on the epilepsy and its management. In fact, comorbidities do not simply affect quality of life of patients but also represent prognostic markers and affects health costs resulting in increased hospitalisation rates, longer hospital length of stay, frequent health-care visits and, ultimately, higher health-related costs [5].

In order to develop successful therapeutic interventions and prevention strategies, it is important to have a clear understanding of the pathophysiology of comorbidities and the magnitude of the problem. The identification, treatment and prevention of comorbidities should become an integral part of epilepsy care and epilepsy centres should lead on the development of treatment guidelines, prevention policies and structured referral pathways for the management of these conditions that can be easily implemented by Neurologists in everyday clinical practice.

This series of articles will explore some among the most frequent and sometimes challenging comorbidities in epilepsy. Focus will be on current research and clinical management. These articles are authored by distinguished experts in the field. I do hope that these articles will stimulate further interest in this area, leading to constant improvements in the care of our patients.

References

1. Keezer MR, Sisodiya SM, Sander JW. Comorbidities of epilepsy: current concepts and future perspectives. Lancet Neurol. 2016;15:106-115. https://doi.org/10.1016/S1474-4422(15)00225-2
2. Scheffer IE, Berkovic S, Capovilla G, et al. ILAE Classification of the Epilepsies Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58:512-521. https://doi.org/10.1111/epi.13709
3. Feinstein AR. The pre-therapeutic classification of co-morbidity in chronic disease. Journal of Chronic Diseases. 1970;23:455-468. https://doi.org/10.1016/0021-9681(70)90054-8
4. Mula M. The Comorbidities of Epilepsy. London: Academic Press; 2019.
5. Patel RS, Elmaadawi A, Mansuri Z, et al. Psychiatric Comorbidities and Outcomes in Epilepsy Patients: An Insight from a Nationwide Inpatient Analysis in the United States. Cureus. 2017;9:e1686. https://doi.org/10.7759/cureus.1686

Table 1. Types of comorbidities of epilepsy

Type	Mechanism	Examples	Management
Causative	One is the cause of the other	Stroke; Traumatic brain injury; CNS infections (eg. neurocysticercosis, HIV); Multiple sclerosis; Brain Tumours; Heart diseases	Tailored treatment strategies; prevention of drug-drug interactions
Reciprocal	One is associated with increased risk of developing the other and vice versa (complex multifactorial reasons)	Mood and anxiety disorders; Psychosis; ADHD; Autism Spectrum Disorder; Irritable bowel syndrome; Headaches; Psychogenic non-epileptic seizures; Diabetes; Suicide	Screening for early diagnosis and management
Mutual	Shared risk factors or aetiological mechanisms	Tuberous sclerosis; Cerebral palsy; Autoimmune encephalitis; Intellectual disabilities; Anti-GAD antibody associated type 1 diabetes; Dementia; Headaches; Heart diseases	Precision medicine and disease modifying agents
Resultant	Caused by seizures and their treatments	Sexual dysfunction; Obesity; Osteoporosis; Heart diseases; Obstructive sleep apnoea syndrome; Type 2 diabetes	Screening and prevention strategies
Coincidental	By chance	Any condition	Tailored treatment strategies; prevention of drug-drug interactions

HIV=Human immunodeficiency virus; ADHD=attention deficit hyperactivity disorder; CNS=Central nervous system; GAD=glutamic acid decarboxylase