



# Epilepsy and Associated Comorbidities

Tianfu Li<sup>1-3,†</sup>

## Abstract

There are several different types of comorbidities exist in epilepsy. Cognitive comorbidities are learning problems that cause difficulty in school and can have lasting effects on educational and professional success; Psychiatric comorbidities are behavior and mood problems including attention deficit disorder, depression, anxiety disorders and combinations of these conditions. Comorbidities in epilepsy impair patients' health-related quality of life and may affect the clinical course of epilepsy. Comorbidities and epilepsy have a bidirectional relationship, sharing common underlying pathogenesis. This special issue updated readers with some of the most recent and exciting progresses including mechanisms, evaluation biochemical biomarkers for epilepsy and comorbidities as well as therapy aim to modify the progression of epilepsy (disease modification) and concomitant comorbidities through by targeting the disease process. It is hoped that such advances in cognitive neuroscience and psychiatry will translate into routine epilepsy clinical practice and provide markers of disease and more targeted treatments. The potential limitations and future efforts with open questions were also offered to stimulate the further research endeavors in the field.

## Keywords

Epilepsy, Comorbidities, Neuropsychiatric, Cognitive, Quality of life

## Introduction

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition [1]. Up to 30 percent of patients with epilepsy is pharmacoresistant [2], and apart from those who are candidates for resective surgery, most will continue to have disabling seizures and the poor quality of life with a wide range of cognitive and psychiatric symptoms [3,4]. Currently, the bidirectional relation between epilepsy and associated comorbidities has been paid much more attentions [5,6], and advances on the overlap of psychiatric and neurologic symptoms from a pathophysiologic and phenomenologic perspective is becoming a hot

topic in epilepsy. In the future, it is feasible to combine neurocognitive and neuropsychiatric markers, allowing systematic advances in our understanding of the natural history of cognitive and behavioral disturbances in the epilepsies relative to the onset and progression of seizures [6].

Epilepsy as prototype of neurocognitive illness, epilepsy associated neurocognitive comorbidities are usually frequent and share common underlying mechanisms with epilepsy. The comorbidities are attributable to recurrent seizures and medications. In fact, the most recent research indicates that some neurocognitive and psychological comorbidities as well as structural brain changes predate the onset of seizures, with the early cognitive compromise being further

<sup>1</sup>Department of Neurology, Epilepsy center, Beijing Sanbo Brain Hospital, Capital Medical University, Beijing, China

<sup>2</sup>Beijing Institute for Brain Disorders, Beijing, China

<sup>3</sup>Beijing Key laboratory of Epilepsy, Beijing, China

<sup>†</sup>Author for correspondence: Tianfu Li, M.D., Ph D., Professor and Chief Physician in Neurology, Vice director of Brain Institute, Beijing Sanbo Brain Hospital, Capital Medical University, Xiangshan Yikesong 50, Haidian district, Beijing, 100093, China. Tel: +86 1062856761; Fax: +86-10-62856902, email: tianfuli66@126.com

magnified by the onset of epileptogenesis, and later on, by the chronicity of seizures [7-10]. Therefore, the comorbidities need to be addressed early in the course of the illness as they have a profound impact on the quality of life and complicate the therapeutic management of epilepsy. It is now strongly recommended that all newly diagnosed patients be screened and tracked for timely intervention. However, major developments in cognitive neuroscience and the vast number of clinical studies on epilepsy, cognition and mind have not found their way into routine clinical practice currently [6].

Epilepsy also as prototype of neuropsychiatric and illness, epilepsy associated neuropsychiatric comorbidities are usually frequent and share common underlying mechanisms with epilepsy. Depressive disorders are the most common type of psychiatric comorbidity in patients with epilepsy, with lifetime prevalence rates of around 35% in population-based studies [11], especially in individuals suffering from refractory temporal lobe epilepsy [4,11]. The epidemiologic observation infers concurrent presence of depression and attention-deficit/hyperactivity disorder (ADHD) in some patients with epilepsy. Such triple morbidity (epilepsy-depression-ADHD) would have obvious diagnostic and therapeutic implications. There is a bidirectional relationship between epilepsy and psychiatric disorders, implying that either of them can antedate or follow mutually, and the modification of one may increase the risk for the development of the other [12,13].

In this special issue, we are delighted to present the invited papers to highlight the recent achievements in epilepsy and associated comorbidities. The major topics in this issue include (1) comorbidities of refractory epilepsy and the update mechanism, (2) microRNAs in the pathophysiology of epilepsy and associated comorbidities, (3) abnormal brain network in epilepsy and associated comorbidities, (4) schizophrenia-like psychosis of epilepsy, (5)

mechanisms of vagus nerve stimulation for epilepsy and associated comorbidities, (6) mechanisms of deep brain stimulation for epilepsy and associated comorbidities, (7) efficacy of deep brain stimulation in the treatment of epilepsy and associated comorbidities. (8) Age effect on cognition improvements after unilateral anterior temporal lobectomy in adults with temporal lobe epilepsy, (9) efficacy of foci resection and bipolar electrocoagulation on functional cortex in the treatment of epilepsy and associated comorbidities in tuberous sclerosis complex.

---

## Concluding Remarks

In conclusion, the special issue updates readers with some of the most recent and exciting advances and developments in epilepsy and associated comorbidities. The papers in this special issue also discuss the potential limitation of the results and address some of the open questions in the field. We hope that these publications are able to provide novel and insightful information to readers further understanding of the relationship between epilepsy and several comorbidities, evaluating physiological, neuroimaging, biochemical biomarkers, as well as strategies for managing comorbidity of psychiatric illness and epilepsy.

---

## Acknowledgements

*We are grateful to the outstanding contributions of the authors for their efforts and collaboration to submit their manuscripts to this special issue. We acknowledge the financial support from national natural science foundation of China (81571275), BIBD-PXM2013\_014226\_07\_000084, National Key Technology R&D Program of China (2012BAI03B02), Scientific Research Common Program of Beijing Commission of Education (KM201410025027), Capital Characteristic Clinical Application Research (Z131107002213169), the capital health research and development of special (2016-4-8011).*

---

## References

1. Fisher RS, van Emde BW, Blume W, *et al.* Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 46(4), 470-472 (2005).
2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N. Engl. J. Med* 342(5), 314-319 (2000).
3. Witt JA, Helmstaedter C. Cognition in epilepsy: current clinical issues of interest. *Curr. Opin. Neurol* 30(2), 174-179 (2017).
4. Kanner AM. Can neurobiological pathogenic mechanisms of depression facilitate the development of seizure disorders? *Lancet. Neurol* 11(12), 1093-1102 (2012).
5. Kumar U, Medel-Matus JS, Redwine HM, *et al.* Effects of selective serotonin and norepinephrine reuptake inhibitors on depressive- and impulsive-like behaviors and on monoamine transmission in experimental temporal lobe epilepsy. *Epilepsia* 57(3), 506-515 (2016).
6. Wilson SJ, Baxendale S. Reprint of: The new approach to classification: Rethinking cognition and behavior in epilepsy. *Epilepsy. Behav* 64(B), 300-303 (2016).

7. Hermann B, Jones J, Sheth R, *et al.* Children with new-onset epilepsy: neuropsychological status and brain structure. *Brain* 129(10), 2609-2619 (2006).
8. Ostrom KJ, Smeets-Schouten A, Kruitwagen CL, *et al.* Not only a matter of epilepsy: early problems of cognition and behavior in children with "epilepsy only"--a prospective, longitudinal, controlled study starting at diagnosis. *Pediatrics* 112(6-1), 1338-1344 (2003).
9. Hermann BP, Jones JE, Jackson DC, *et al.* Starting at the beginning: the neuropsychological status of children with new-onset epilepsies. *Epileptic. Disord* 14(1), 12-21 (2012).
10. Hermann BP, Dabbs K, Becker T, *et al.* Brain development in children with new onset epilepsy: a prospective controlled cohort investigation. *Epilepsia* 51(10), 2038-2046 (2010).
11. Tellez-Zenteno JF, Patten SB, Jette N, *et al.* Psychiatric comorbidity in epilepsy: a population-based analysis. *Epilepsia* 48(12), 2336-2344 (2007).
12. Hesdorffer DC, Hauser WA, Olafsson E, *et al.* Depression and suicide attempt as risk factors for incident unprovoked seizures. *Ann. Neurol* 59(1), 35-41 (2006).
13. Srinivas HV, Shah U. Comorbidities of epilepsy. *Neurol. India* 65(1), S18-S24 (2017).