



Review

How neuropsychology can improve the care of individual patients with epilepsy. Looking back and into the future[☆]



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ABSTRACT

Some of the roots of current clinical neuropsychology go back to the early days of epilepsy surgery. Looking back a huge number of publications have dealt with cognition in epilepsy. The major factors driving this work were questions relating to surgery, antiepileptic drugs and, more recently, also to underlying pathology. However, most factors affecting cognition in epilepsy have been discerned many years ago. The body of neuropsychological literature in this field has accumulated much knowledge, raising the question why, apart from epilepsy surgery settings, neuropsychology has still not been fully integrated in the routine care of patients with epilepsy. This review on the occasion of *Seizure's* 25th anniversary attempts to summarize clinically relevant diagnostic advances following a question guided, modular, and evidence-based approach. In doing so, we hope to attract the interest of readers to an exciting mode of assessment which does not only have theoretical but also practical relevance. The comorbidities of epilepsy are becoming an increasingly relevant topic. It is now widely accepted that, while epilepsy may be defined by the occurrence of epileptic seizures, these seizures represent only one of several possible sources of cognitive impairment. It is well-established that there are complex interactions between epilepsy, cognition and behavior, and that both seizures and problems with cognition or behavior may result from a common underlying pathology requiring treatment. With this review we aim to demonstrate that neuropsychology can make a highly valuable contribution to the care of individual patients by contributing to the diagnostic process and by serving as a tool for the monitoring of disease and treatment, thereby improving the quality and safety of patient care. On a national, European, and international level, first efforts are being made to homogenize diagnostics across epilepsy centers and countries in order to achieve a common language and core standards. This should improve communication within and outside the speciality, and help to generate the data required to allow the field to make further progress.

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1. Introduction

Nearly 30 years ago, Michael Trimble, in an article published in *Epilepsia*, described the cognitive hazards of seizure disorders, identifying the major factors to be considered with cognitive impairment in epilepsy in two groups of patients with this disorder, i.e. underlying brain damage, age at seizure onset, seizure type and frequency, as well as antiepileptic drugs (AEDs) [1].

He was not the first to raise the question of what the reason for cognitive deficits in epilepsy may be, but this early study already revealed an understanding of the complex and multifactorial etiology of cognitive impairment and decline in epilepsy. The question of mental impairment and decline in epilepsy is old and was discussed as “epileptic dementia” in medical texts as early as at the turn of the 19th century [2–4]. At that time, with reduced knowledge about the different structural, metabolic, and genetic causes of epilepsy, epileptic dementia was thought to manifest in 50% of all patients. Interestingly, the mental problems were mainly attributed to what was considered as non-lesional epilepsy in these days. While it should be pointed out that the term “dementia” is used differently today (when it specifically refers to progressive mental decline) these early writings demonstrate that, although seizures were the main focus of medical interest,

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cognitive and behavioral (personality) abnormalities were well-recognized and thought to be directly linked to the disorder.

Stimulated by the success story of epilepsy surgery starting in 1935 [5] and by new antiepileptic drug developments from the 1960s and 70s, a large body of neuropsychological research on cognition and epilepsy has accumulated over the past decades [6]. With an increasing understanding of the mechanisms underpinning the epilepsies, etiological models of cognitive impairment in the epileptic disorders became more elaborated, but the basic determinants are still the underlying static versus dynamic brain pathology, epileptic activity (both in terms of seizures and interictal epileptic dysfunction), psychiatric comorbidity and treatment effects [7]. In addition, newer models underline the relevance of personal and sociocultural variables as well as, most importantly, the neurodevelopmental context (i.e. differences between the developing versus the ageing brain). Along with progress in brain imaging, neuropathology and genetics, the number of epilepsies with an unknown etiology has reduced significantly, prompting changes in seizure and epilepsy classifications but also the appreciation of the cognitive impairments in epilepsy [8]. In contrast to a traditional epilepsy-centric view according to which cognitive impairments and behavioral problems are the result of having seizures, new etiological models increasingly consider neuropsychological problems as one of several comorbidities of epilepsy [9,10]. Cognitive impairment can be the consequence of epilepsy but can precede the development of epilepsy as well, and epilepsy and cognitive impairment can both be comorbidities resulting from the same underlying pathology [11]. The major consequence for clinical practice is that it is not sufficient to treat seizures to resolve the cognitive problems seen in patients with epilepsy. Neuropsychology represents an independent approach to the patient, his disorder and its underlying pathology and may call for therapeutic interventions other than those primarily directed at reducing the number of seizures.

On the basis of this theoretical framework, what follows in this review is a discussion of the highly relevant question of how, thirty years after Michael Trimble's work, and after 80 years of epilepsy surgery, accumulated neuropsychological knowledge does or does not translate into the routine care of individual patients. We will consider this question in relation to neuropsychological diagnostics, monitoring of the disorder and its treatment, patient counseling, and therapeutic decision-making.

2. Advances in diagnostics

UCB and John Libbey sponsored a meeting in Toronto, Canada, on 3–6 November, 2010, involving 66 specialists from 13 countries representing expertise in adult and pediatric neuropsychology, psychiatry, and neurology; neuroimaging, cognitive neurosciences, electrophysiology, pharmacology, and other fields. The overarching idea and very practical aim of the meeting was to disseminate evidence-based neuropsychological practice in the care of children and adults with epilepsy around the world.

It became evident that standardized neuropsychological assessment has become an integrated and essential tool in the diagnostic and clinical evaluation of patients considering epilepsy surgery. However, there was a great heterogeneity of assessments and their application, and despite progress in other diagnostic fields and in the treatment of epilepsy, clinical neuropsychology in epileptology still appeared to be very focused on epilepsy surgery, especially temporal lobe surgery. There was little indication that it had secured a clear role in the routine care of patients with epilepsy outside epilepsy surgery evaluation. At that time Medline listed as many as 3000 publications under the search "epilepsy and cognition". Thus, major developments in cognitive neuroscience and the vast number of clinical studies on epilepsy, cognition and mind, had obviously not found their way into routine clinical practice. One of the outcomes of the Toronto meeting was the publication in the *Progress of Epileptic Disorders Series* by John Libbey in 2011. This publication continues to be a very comprehensive compendium which provides an overview of the state of the art at that time [12].

Following this publication and an inquiry of all members of the ILAE Neuropsychology Task Force, Bruce Hermann, Madison Wisconsin, who was one of the organizers of the Toronto meeting and the leader of the Task Force at that time, summarized the strategy for the future as listed in [Table 1](#).

Meanwhile the ILAE task force, now under the leadership of Sarah Wilson, University of Melbourne, Australia, has published a consensus paper on the indications for and expectations of neuropsychological assessment in routine epilepsy care [13]. The paper addresses what the role of neuropsychological assessment is, who should carry out a neuropsychological assessment, when people with epilepsy should be referred for neuropsychological assessment, and what can be expected from it. This

Table 1

Future tasks for neuropsychology in epilepsy (as formulated in 2011).

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1. Top priority: Definition of optimal cognitive and behavioral measures for screening epilepsy-related impairments in different types of epilepsy (i.e. epilepsies with different etiologies), and to define . . .
 - measures for assessment of developmental disorders
 - measures for acute symptoms and confusional states in status epilepticus, inflammation (encephalitis), mitochondrial diseases, etc.,
 - measures sensitive to antiepileptic drug treatment,
 - measures sensitive to EEG pathology (electrophysiological epileptic activity, single spikes & spike waves, grouped activity, nonconvulsive (cognitive) seizures) and sensitive to reflect successful treatment of the EEG
 - common protocols for assessment of hemispheric dominance (intracarotid amobarbital test (IAT), functional MRI (fMRI), functional transcranial Doppler sonography (fTCD), dichotic listening)
 - measures sensitive to surgical treatment,
 - measures and markers for assessing every day functioning
 2. Secondary aims were . . .
 - to come to an agreement on core screening tests or tools for a test battery,
 - to identify national (language) and cultural needs,
 - to find multicenter, multi-language, and transcultural solutions,
 - to find new avenues for disseminating methods, techniques and normative data,
 - and to have maybe another meeting to envisage the completion of this action.
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