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Review

Nonconvulsive status epilepticus

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Abstract

Nonconvulsive status epilepticus (NCSE) is a heterogeneous disorder with multiple subtypes. Although attempts have been made to define and classify this disorder, there is yet no universally accepted definition or classification that encompasses all subtypes or electroclinical scenarios. Developing such a classification scheme is becoming increasingly important, because NCSE is more common than previously thought, with a bimodal peak, in children and the elderly. Recent studies have also shown a high incidence of NCSE in the critically ill. Although strong epidemiological data are lacking, NCSE constitutes about 25–50% of all cases of status epilepticus. For the purposes of this review, we propose an etiological classification for NCSE including NCSE in metabolic disorders, NCSE in coma, NCSE in acute cerebral lesions, and NCSE in those with preexisting epilepsy with or without epileptic encephalopathy. NCSE is still underrecognized, yet potentially fatal if untreated. Diagnosis can be established using an electroencephalogram (EEG) in most cases, sometimes requiring continuous monitoring. However, in comatose patients, diagnosis can be difficult, and the EEG can show a variety of rhythmic or periodic patterns, some of which are of unclear significance. Although some subtypes of NCSE are easily treatable, such as absence status epilepticus, others do not respond well to treatment, and debate exists over how aggressively clinicians should treat NCSE. In particular, the appropriate treatment of NCSE in patients who are critically ill and/or comatose is not well established, and large-scale trials are needed. Overall, further work is needed to better define NCSE, to determine which EEG patterns represent NCSE, and to establish treatment paradigms for different subtypes of NCSE.

Keywords: Status epilepticus; Nonconvulsive status; Nonconvulsive status epilepticus

1. Introduction

Status epilepticus was described in the early 1800s by French and English physicians using various names such as *furor epilepticus*; *epileptic mania*, *epileptic delirium*, and *fureur epileptique*. Additionally, the term *petit mal intellectual* was used in France in the mid-1800s [1]. The advent of EEG has allowed distinction between the different forms of status epilepticus, with the first description of absence status by William Lennox in 1945 and of complex partial status epilepticus by Gastaut in 1956 [1]. The concept of nonconvulsive status has evolved over the last 50 years with descriptions of "spike–wave stupor" by Niedermeyer and Khalifeh [2] and the differences in "subtle versus overt" status epilepticus described by Treiman and colleagues [3].

Nonconvulsive status epilepticus (NCSE) is now known to be a heterogeneous disorder with varied etiology and several subtypes. It is a common yet still underrecognized condition, especially in critically ill and comatose patients. Delay in diagnosis and treatment may be associated with increased mortality. However, there is still no universally accepted definition. There is also disagreement on the electroencephalographic features that are consistent with NCSE and confusion on how aggressively it should be treated, especially in patients who are critically ill and/or comatose.

In this review, we discuss the various aspects of the disorder across the life span, including nosology, definitions, and epidemiology in various age groups. We then outline

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the classification schemes that can be used and propose an etiological classification. We also outline the pathophysiology; neuropsychological consequences of the disorder, and various EEG patterns associated with NCSE. Finally, we discuss the principles of treatment for NCSE.

2. Nosology and definition

A variety of terms have been used in the literature to denote NCSE, including *minor status epilepticus, spike–wave stupor, epileptic twilight state, epilepsia minores continua, petit mal, impulsive-petit mal status,* and *dialeptic status epilepticus*, to name a few [4]. None of the terms accurately encompasses all the features of NCSE, which can be varied. For example, petit mal status may simply denote absence status epilepticus. Spike–wave stupor has been used to denote a specific EEG pattern [2]. Subtle convulsive status is a term used to describe status epilepticus with subtle clinical features of myoclonic jerks or nystagmus in association with electrographic discharges [3]. Epileptic twilight state is a term used in the setting of complex partial status epilepticus [5]. Dialeptic status is a term that incorporates semiology into classification [6]. None of the preceding terms are universal, as the condition encompasses diverse clinical, etiological, and EEG features, and thus the term NCSE is currently accepted terminology with the understanding that there are many subtypes.

There are no current universally accepted definitions of NCSE. The definition of NCSE cannot rely on clinical symptoms alone because they may range from subtle encephalopathy and subtle clinical signs to a frank comatose state. Moreover, clinical symptoms may be indistinguishable from those of other nonepileptic disorders, for example, transient global amnesia [7]. Definitions cannot rely simply on EEG criteria because there are no EEG patterns that are pathognomonic of NCSE, which can range from continuous ictal discharges that may be focal or generalized to rhythmic and periodic patterns of undetermined significance. Definitions cannot be based on duration alone either. Most epidemiological studies of status epilepticus have specified a duration of 30 minutes, though this is completely arbitrary. Response to treatment can be considered a part of the definition, though lack of immediate response to treatment does not necessarily exclude the diagnosis. We propose that from a practical standpoint, a working definition should consist of all of the aforementioned aspects. Thus, NCSE can be defined as a condition with a prolonged state of impaired consciousness or altered sensorium associated with continuous paroxysmal activity or electrographic discharges on the EEG.

3. Epidemiology

The incidence of NCSE varies according to age and subtype. However, general population-based incidence rates are difficult to obtain for NCSE given the fact that incidence varies across age groups. Moreover, existing studies use different diagnostic criteria and definitions for NCSE. Furthermore, data are mostly from tertiary care centers in which some selection bias exists and, therefore, difficult to extrapolate to the general population.

Incidence rates for status epilepticus (including all types) vary in epidemiological studies from 9.9/100,000 per year in adults to 54.2/100,000 per year in the elderly [8–12]. Cumulative incidence of status epilepticus, which includes both convulsive and nonconvulsive status, has been studied both in Europe and in the United States. European studies show incidence rates from 9.9/100,000 in French-speaking Switzerland [10] to 10.7 in Bologna, Italy [12] and 17.1 in Germany [11]. In the United States, two studies examined the incidence of status epilepticus. In a cohort from Rochester, MN, the incidence rate was 18.3 [9], and in another prospective study in Richmond, VA, rates were higher at 41/100,000 per year [8]. The causes underlying such variation are not clear, though differences in case ascertainment may account for it. The incidence of both convulsive and nonconvulsive status in these studies has a bimodal distribution, with the highest incidence in children less than 1 year of age and in the elderly over the age of 60.

There are no epidemiological studies specifically examining the population-based incidence of NCSE. However, several studies have examined NCSE in the critically ill. Knake et al. [11] point out that NCSE constitutes about 25–50% of all cases of status epilepticus. In a prospective study of comatose patients in the ICU without overt clinical signs, Towne et al. [13] found that 8% of patients had NCSE on the basis of the EEG. Others have reported prevalences of 31 and 38% for NCSE in comatose adults in ICU. In another prospective study, Litt et al. [14] showed that about 0.5% (24 of 4559 patients over 2 years) of elderly admitted to the medical ICU have NCSE. In the neurological ICU, the prevalence may be higher, with 22 of 210 (10.5%) patients having NCSE either on an emergent EEG or following continuous EEG monitoring [40]. The prevalence of nonconvulsive seizures (not necessarily NCSE) may be even higher. Claassen et al. [15] found that 18% of patients who underwent continuous EEG monitoring in the ICU had nonconvulsive seizures. However, all of these studies have a selection bias, which may have inflated the incidence rates.

Prevalence estimates for NCSE in the elderly are much higher than those in young adults. Epidemiological studies from both Europe and the United States report a much higher prevalence of status epilepticus in the population over age 60. Age-adjusted prevalence rates averaged 54.5/100,000 in the German study [11], though this included both convulsive and nonconvulsive status epilepticus. In the Rochester cohort as well, the incidence of status was much higher in elderly over the age of 65 (>50/100,000) and children under 1 year of age compared with adults younger than 65 [9]. Finally, the incidence rate for patients over 60 for status epilepticus of all types is 15/100,000 per year in Finland [10].