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Watch the language! Language and linguistic-cognitive abilities in children with nocturnal epileptiform activity

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ABSTRACT

We studied the language and linguistic-cognitive abilities of a group of children with nocturnal epileptiform activity (NEA; N = 33) who were hospitalized at a tertiary epilepsy hospital. The children were compared with two groups: one age- and gender-matched group (N = 33) and one group matched on language ability (vocabulary) and gender (N = 66). We also examined how NEA-related variables affected language abilities. Overall, the children with NEA showed delayed language abilities and a trend for specific difficulties with phonology and naming speed. We did not find firm evidence that the amount of NEA, the use of antiepileptic drugs (AEDs), and the lateralization and localization of NEA had an effect on language. However, we found that children with right-lateralized epileptiform activity seemed to have specific difficulties with naming speed. Additionally, our results indicated that NEA located in the centrotemporal areas particularly affected phonology and orthographic skills.

1. Introduction

Nocturnal epileptiform activity (NEA) describes interictal discharges during sleep without concurrent epileptic seizures; hence, it is only detectable on EEG. In this article, we use the term NEA as a broad concept that is not limited to a specific quantity. NEA occurs in several epileptic syndromes that are sometimes referred to as a spectrum of conditions, including benign childhood epilepsy with centrotemporal spikes (BECTS), Landau Kleffner syndrome (LKS) and continuous spike and waves during sleep (CSWS); however, it may also be present in children without any known epileptic syndrome or epileptic seizures, such as children with language impairment [1]. The presence of a considerable amount of NEA, traditionally understood as above 50–85% of non-REM sleep, is commonly called electrical status epilepticus during sleep (ESES) [2]. NEA is an age-dependent condition, meaning that both onset and recovery are confined to childhood [3].

Syndromes with NEA are often accompanied by cognitive, behavioral, and/or academic impairments [4–6]. Some children with NEA also experience regression of previously acquired skills [7]. Impairments associated with NEA conditions are argued to lie along a continuum of severity [3]. It is described that children with CSWS have global impairments, those with LKS experience impairments restricted to language, and those with BECTS show milder impairments [6]. Some researchers have argued that language skills are particularly affected in children with NEA [8].

There is an ongoing debate concerning NEA's causative role in the abovementioned impairments. Research showing that the amount of NEA corresponds to the severity of impairments [9,10], and studies that demonstrate that the localization and/or distribution of NEA relates to the nature of the difficulties [11–13] could be taken as evidence supporting the causative role of NEA. It is furthermore described that the cognitive consequences of NEA could depend on brain maturation at NEA onset [14]. Several study results are difficult to interpret. For instance, difficulties within cognitive domains prior to the onset of NEA [15] could be taken as evidence of a shared underlying cause of cognitive impairments and NEA. Considering the (concurrent) subclinical nature of NEA, the onset of NEA is difficult to determine. In other words, the cognitive consequences of NEA could persist for some time before NEA is confirmed. Thus, cognitive difficulties (for instance language impairment) could be the first symptom of NEA. Additionally, findings of impairments that persist after NEA ceases could indicate that NEA disturbs brain development in a fundamental and long-lasting way [16]. Persistent impairments could also reflect a cardinal cause of both the impairments and the NEA.

The mechanisms of the relationship between NEA and cognitive impairments are not yet fully understood. A frequently cited theoretical explanation postulates that NEA affects memory by interfering with consolidation processes during sleep [17]. More than that, the theory of remote inhibition proposes that the metabolic disruption

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induced by NEA is conducive to the regression of cognitive skills [18]. Fernández et al. [3] suggest that the underlying cause of NEA and several other pathophysiological mechanisms could influence cognitive development in complex ways.

Although children with NEA often seem to have impairments related to the language or linguistic-cognitive areas, there is no clear understanding of the relationship between language abilities and NEA in this group [1], and Fandino et al. [19] point to the fact that literature, on LKS, from the field of speech language pathology is sparse.

The aim of the present study was therefore to extensively study whether and how the language abilities of children with NEA differ from those of typically developing children. To do this, we examined language and linguistic-cognitive skills, as well as general abilities. We also investigated how NEA-related factors, such as the NEA amount, number of antiepileptic drugs (AEDs), and the lateralization and localization of the epileptiform activity affected language abilities. By excluding children with an active seizures and those with a diagnosis known to cause language impairment (cerebral palsy, autism and mental retardation) but not excluding specific epileptic syndromes, we studied children with one phenomenon in common, namely NEA. The study focused on the effect of epileptiform activity during sleep in that we included only children with an increase in epileptiform activity from the wake state to the sleep state. Moreover, because there are unclear relationships between the amount of NEA and the degree of difficulties, NEA was not restricted to a defined quantity. We compared the children with NEA to two groups of typically developing children. By including both an age-matched and a language-matched comparison group, we could examine whether the difficulties of the children with NEA were delayed or deviant. In other words, when comparing children with NEA to children matched on a specific language ability, we should expect similar results for the remaining abilities if the children with NEA only have delayed impairments.

Two main questions were put forward in the present study. To support us in answering these questions, we formulated the following hypotheses:

- In what ways do the language abilities of children with NEA differ from those of typically developing children?
  1. Children with NEA have specific challenges with language and not with nonverbal abilities.
  2. Children with NEA have delayed language abilities and not deviant language abilities.
- How do NEA-related factors affect the language abilities of children with NEA?
  1. NEA-related factors (amount of NEA, number of AEDs, lateralization and localization) affect the language abilities of children with NEA.

2. Methods

2.1. Participants

Three groups of monolingual Norwegian children were included in this study: one patient group and two comparison groups (chronological age-matched and language ability-matched). The children should not have any known diagnosis (such as cerebral palsy, autism or mental retardation), except for epilepsy in the NEA group. In addition, the comparison groups should not have been referred to the Educational and Psychological Counselling Service before or at study inclusion.

The patient group (NEA group) consisted of 33 children (26 males) ranging in age from 4 to 10 years (mean age 99.58 months (SD: 20.63, min-max: 49–131)). The majority of the children were 9 and 10 years old. The participants were recruited from the National Centre for Epilepsy in Norway between autumn 2011 and spring 2015, regardless if it was their initial stay at the hospital or a follow-up. Children admitted to this center could be referred for reasons other than epileptic seizures: For example, children with cognitive difficulties could be referred for 24 h-EEG with questions about NEA. All children in the NEA group underwent 19-channel ambulatory EEGs. The recording length was in the range of 18–23 h. An experienced neurophysiologist interpreted all EEGs by visual inspection. In accordance with previous studies conducted at the center [20], children were invited to participate in the study if epileptiform activity increased more than four times from daytime to sleep state. The amount of spikes in daytime was obtained by finding an artifact-free period in the afternoon and compared to the amount of spikes in the first sleep cycle. We did not have a lower limit for NEA; thus, we included all children with a four-fold increase, even if the NEA amount was low. Furthermore, the children should have been seizure-free for the last 6 weeks before study inclusion to avoid measuring the possible temporary impact of seizures on cognition. We had no access to further information about seizure history. Additionally and in line with other studies, we did not exclude children with ADHD [21]. The children in the NEA group had the following epilepsy diagnoses: BECTS (N = 7), atypical BECTS (N = 1), LKS (N = 3) and CSWS (N = 1). Twenty-one children did not have any epilepsy diagnosis except NEA. Four children were not medicated with AEDs. In addition, three children were medicated for ADHD.

The children in the chronological age-matched comparison group (CA group) were matched with the children with NEA on age and gender (N = 33, mean age: 99.36 months (SD: 20.57, min-max: 49–131)) and were recruited in two ways. First, for each child with NEA who had attended school for more than half a year, a CA child was recruited from a school in a suburban district. Second, for the younger children with NEA, the CA children were drawn from a cohort. The cohort was part of a large-scale longitudinal study that included children at age four years and who were tested yearly until age nine years. If there was no child with the same age in months as a child with NEA, the CA-matched child was selected alternately from those one month younger and those one month older.

The children in the language ability-matched comparison group (LA group) were matched with the children with NEA on a vocabulary measure (BPVS raw-score) and gender. We chose two LA-matched children for each child with NEA (N = 66, mean age: 80.95 months (SD: 12.10, min-max: 50–92)). The LA group was drawn from the cohort mentioned above. We included children from the first four test points only because the tests administered at those points coincided with the tests given to the children with NEA. To ensure that the LA group consisted of typically developing children, the vocabulary score had to lie within the range of normal variation. In other words, no children included in the LA group had vocabulary scores that exceeded 1.5 SD from the cohort's mean score on the respective test points. If there was no cohort child with an identical score, the LA children were selected alternating one score down and one score up.

2.2. Procedure, NEA group

To be included in the study, a four-fold increase, or more, in epileptiform activity from the wake state to the sleep state was required on EEG (inclusion EEG). For 21 children, inclusion EEG and testing took place at the same hospital stay. The remaining children were tested either during their subsequent hospitalization (N = 8) or at their home school by the first author (N = 4). We hypothesized that normalization of the EEG would not lead to immediate cognitive improvements. Therefore, we planned to test the children even when the EEG had normalized. Seven children had normalized EEGs at the time of language and linguistic-cognitive testing, whereas five children did not have an EEG at the time of testing. Of the children with normalized EEGs, four had an epilepsy