



Psychiatric comorbidity in children and youth with epilepsy: An association with executive dysfunction?



Kristin Å. Alfstad^{a,*}, Halvor Torgersen^a, Betty Van Roy^b, Erik Hessen^{a,c,i}, Berit Hjelde Hansen^d,
Oliver Henning^a, Jocelyne Clench-Aas^e, Petter Mowinckel^f, Leif Gjerstad^{g,h}, Morten I. Lossius^a

^a National Centre for Epilepsy, Division for Surgery and Clinical Neuroscience, Oslo University Hospital, Norway

^b Department of Pediatrics and Adolescent Medicine, Akershus University Hospital, Lørenskog, Norway

^c Department of Neurology, Akershus University Hospital, Lørenskog, Norway

^d Division of Mental Health, Akershus University Hospital, Lørenskog, Norway

^e The National Institute of Health, Department of Mental Health, Norway

^f Department of Paediatrics, Oslo University Hospital, Norway

^g Department of Neurology, Division for Surgery and Clinical Neuroscience, Oslo University Hospital, Norway

^h Faculty of Medicine, University of Oslo, Norway

ⁱ Department of Psychology, University of Oslo, Norway

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ABSTRACT

Objectives: Psychopathology in children and youth with epilepsy has previously been related to executive dysfunction, but the nature of the association is uncertain. We sought to explore risk factors for psychiatric disorders in children and youth with epilepsy, with emphasis on executive dysfunction, along with seizure-related and psychosocial factors.

Methods: The cohort consisted of one hundred and one consecutive patients aged 10–19 years with focal ($n = 52$) or genetic generalized ($n = 49$) epilepsy. All were screened for psychiatric symptoms, using part of an extensive questionnaire, the Strengths and Difficulties Questionnaire (SDQ) for both patients and their parents. Participants scoring in the borderline or abnormal range on the SDQ received a psychiatric interview (Kiddie-SADS-PL). All participants underwent a neuropsychological examination, and those with general cognitive abilities ($IQ < 70$) were excluded.

Results: Forty-seven of 101 participants (46.5%) had a SDQ score in the borderline or abnormal range and underwent a psychiatric evaluation. Of these, 44 (93.6%) met the criteria for a psychiatric diagnosis, the most common being ADHD and anxiety. An executive deficit was identified in 26.8% of the participants with a psychiatric diagnosis, but in only 5.4% of those without such a diagnosis ($p = 0.003$). Multivariate logistic regression analysis showed that executive dysfunction was an independent risk factor for having a psychiatric disorder (OR 8.2, CI 1.8–37.2, $p = 0.006$), along with male gender (OR 2.9, CI 1.2–7.3, $p = 0.02$), and early seizure onset (OR 0.86—that is one year older equals risk of psychiatric disorder reduced by 14%—CI 0.77–0.96, $p = 0.01$). Other epilepsy-related or psychosocial factors were not significantly associated with psychiatric disorders.

Conclusions: Multiple factors are associated with psychiatric problems in children and youth with epilepsy. In this study, executive dysfunction, male gender, and early epilepsy onset were independent risk factors for having a psychiatric disorder. An evaluation of psychiatric and cognitive problems is important to enable a positive long-term outcome in childhood epilepsy.

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1. Introduction

Psychiatric comorbidity affects quality of life in children and youth with epilepsy (CWE) and is important to address in clinical care [1]. Psychopathology occurs frequently, but prevalence rates show a wide variation (21–60%) depending on the population studied and differences in methodology [2]. Identification of risk factors may enable

implementation of preventive measures at an early stage, and this might improve the prognosis.

Different risk factors for behavioral problems in CWE have been investigated, but many questions remain unresolved. Psychiatric problems have been examined in relation to various epilepsy syndromes. Whereas some report more psychopathology in focal epilepsy than in generalized (absence) epilepsy [3], others find no difference between syndromes [4]. Underlying structural brain abnormalities that cause epilepsy have been found to be associated with psychopathology in several studies [5]. Poorly controlled seizures or antiepileptic drug

* Corresponding author. Tel.: +47 67501000.

E-mail address: kristina@ous-hf.no (K.Å. Alfstad).

(AED) polytherapy has also been shown to increase the risk of adverse outcome, but not consistently [2]. Age, gender, and socioeconomic factors are likely to be influential, but even here, findings are inconclusive [2]. The distribution of various psychiatric disorders varies between genders, and some disorders have a later age of onset, contributing to the complex picture. Behavioral deficits may also be present before seizure onset, supporting the importance of neurobiological factors [6].

A cognitive deficit in the domain of executive functions (EFs) has also been found to be a possible factor in behavioral problems in CWE [7]. Neuropsychological function in focal epilepsies has been considered to be closely linked to the region of the brain affected and to mirror the function of that area. However, more widespread deficits are often found. Executive functions, located in the frontal lobe, involve the ability to control and regulate cognition and behavior and to adapt to changing situations. Problems in EF could thus be expected to occur especially in frontal lobe epilepsy (FLE), but such deficits can be found even in temporal lobe epilepsy (TLE) syndromes. For instance, the neuropsychological profile of idiopathic generalized epilepsy, especially juvenile myoclonic epilepsy, shares some common characteristics with FLE [8].

Whether the level of executive function in CWE with psychiatric disorders is lower than that in CWE with no psychiatric disorders is unclear. Our study sought to study this question in a clinically well-defined CWE cohort, with psychiatric interviews providing valid psychiatric diagnoses, complemented by a standardized, well-validated neuropsychological assessment. The aim was to investigate associations between psychiatric disorders and executive dysfunction, along with epilepsy-related and psychosocial factors in children and youth with epilepsy.

2. Methods

2.1. Patient inclusion

Patients aged between 10 years and 19 years were included consecutively in the study during hospital stays at the National Centre for Epilepsy, the only tertiary epilepsy center in Norway, from January 2012 to June 2014. Informed written consent was obtained from parents or participants of legal age; children gave their assent. The patients/parents who declined participation gave written consent that clinical data from their journals could be used by the research group. This enabled comparisons of demographic and epilepsy-specific information between eligible nonparticipants and the study group. The study was approved by the Regional Ethics Committee (2011/1636/REK sør-øst B).

2.2. Clinical data

Participants and parents were interviewed, and all clinical records were extensively reviewed. All but one participant had a 24-hour EEG recording, and video surveillance for seizure detection during sleep is routinely used at the hospital. Electroencephalogram findings were classified as epileptiform activity present or absent during recording. All EEGs were interpreted by a neurologist experienced in neurophysiology.

All participants had MRI, except nine participants with either benign childhood epilepsy with centrotemporal spikes (BECTS) or genetic generalized epilepsies (GGE). The International League Against Epilepsy (ILAE) classification of seizures and epilepsies was used [9].

Two experienced neurologists classified each case independently; interclassification reliability was 93%. For nonconsensus or difficult cases, a child neurologist reviewed the cases.

Genetic generalized epilepsies included were: generalized epilepsy with febrile seizures plus (GEFS+), childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), generalized tonic-clonic seizures (GTCs) only, and GGE not otherwise specified (nos).

Focal epilepsies were classified as: temporal lobe (TLE), frontal lobe (FLE), BECTS, or focal epilepsy from anterior brain regions, but difficult to subclassify (focal epilepsy nos).

Patients with focal epilepsies from the posterior regions (parietal or occipital) were excluded, as were patients with intellectual disability (See Fig. 1 for more details on inclusion and exclusion criteria and examination protocol).

Seizure frequency was dichotomized, and comparisons made between the group of participants that had not experienced generalized tonic-clonic seizures (GTCs) during the previous 6 months and the group of participants that had experienced one or more GTCs during the same period. The numbers of participants on AEDs with possibly the highest potential for cognitive (i.e., phenobarbital, benzodiazepines, topiramate, zonisamide) or behavioral (levetiracetam) side effects were also analyzed [10,11].

Participants and parents completed a 110-item health questionnaire covering different topics, including sociodemographic and psychosocial conditions, school participation and well-being, and physical and mental health. The questionnaire also contained questions on family income and if the children were living with both parents or not. A low-income group was defined as below 60% of the median income in Norway (European Union definition), and the variable “single parent” was used if the child’s parents were not living together.

2.3. Psychiatric evaluation

In order to assess psychiatric symptoms, the Strengths and Difficulties Questionnaire (SDQ), both self (patient) and parent reports, were administered as part of the health questionnaire. The SDQ is a behavioral screening tool, widely used in both epidemiological and clinical studies, and has good psychometric properties [12]. The questionnaire consists of 25 items and can be divided into 5 subscales, covering emotional symptoms, conduct problems, hyperactivity, and peer problems, as well as prosocial behavior. The items can be rated “not true” (0), “somewhat true” (1), or “certainly true” (2), and the scores on the first 4 subscales listed are combined to obtain a total difficulty score (0–40). The total scores can be classified as either “normal”, “borderline”, and “abnormal”. Using British norms (Norwegian norms are not established) on the self report, a score of 0–15 is rated as being in the normal range, 16–19 is borderline, and >19 as abnormal; in the parent report, the corresponding scores are: normal, 0–13; borderline, 14–16; and abnormal, >16. Patients scoring as borderline or abnormal in either the self or parent reports underwent a psychiatric examination for a clinically validated diagnosis. This methodological approach has been previously used also by other research groups [13]. The Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime version (Kiddie-SADS-PL), a semistructured diagnostic interview, was used to assess psychiatric disorders according to DSM-IV criteria [14]. The examinations were performed by one of two experienced child psychiatrists, blinded to SDQ findings. Ten participants were examined jointly by both examiners in order to validate the evaluation. Both patients and parents were interviewed, and the study reports on the prevalence of present diagnoses. The psychiatric diagnoses were grouped as: externalizing (disruptive behavior disorder and substance abuse), internalizing (depressive disorders, anxiety disorders, adjustment and stress disorders), and neuropsychiatric disorders (ADHD, Tourette’s syndrome, tics, obsessive compulsive disorder, psychosis, and autism spectrum disorder).

Patients with a psychiatric disorder requiring further treatment after the hospital stay were referred to the local psychiatric health-care system.

2.4. Neuropsychological assessment

The patients underwent a neuropsychological assessment, with the main focus on three cognitive domains: verbal intelligence, delayed

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