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Review

Social functions and socioeconomic vulnerability in epilepsy

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ABSTRACT

Social functions are commonly impaired in people with epilepsy who are at increased risk of experiencing altered social cognition, communication problems, and interpersonal difficulties. Several factors are implicated, including developmental delay, seizure-related factors, somatic and psychiatric comorbidities, antiepileptic drugs (AEDs), and – not least – the effects of stigma. The variable interaction of all these factors can explain the differing pictures observed in the various epilepsy phenotypes but is also a source of interindividual variability depending on the strength of the effects of each factor on social cognition.
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1. Introduction

Epilepsy is a chronic disorder that can be associated with significant social difficulties resulting in a major public health problem in children and adults [1,2]. The social functions considered at risk in people with epilepsy include, among others, employment, social interactions, family relationships, and experiential activities. Epilepsy has negative effects on social cognition, a high-level cognitive function that includes all the processes used to understand and store information on the interactions with others in a social context [3]. People with epilepsy are at increased risk of having impaired social cognition, communication problems, and interpersonal difficulties [4]. This places a burden on the individual, his/her family members, and on the society at large. A number of factors contribute to the impairment of social competences and ultimately affect social interactions in people with epilepsy. These include disease-related factors (developmental trajectories, structural and functional brain lesions, the occurrence of seizures, antiepileptic drugs (AEDs), and somatic and psychiatric comorbidities) and the effects of stigma. The variable interaction between personal and external factors may result in fewer interpersonal relationships, including lower rates of schooling, employment, leisure activities, marriage, driving, and other types of social engagement, which contribute to social isolation, discrimination, and misconception, and have adverse effects on quality of life [5].

2. Epilepsy: a complex disease with relevant socioeconomic implications

According to the World Health Organization (WHO), a total of 50 million people live with epilepsy in the world [6]. The disease affects both sexes and all ages with worldwide distribution. Epilepsy poses a substantial economic burden for health systems and individuals and their families [7]. The disease is a symptom complex represented by unprovoked seizures that arise from altered brain functions and is secondary to a variety of structural or functional injuries to the central nervous system in about one-half of cases [8]. Several diseases, including, among others, depression, anxiety, dementia, and migraine, are more common in people with epilepsy than in the general population [9]. Along with seizures, these diseases have profound effects on daily living activities and, consequently, relevant social and economic implications, with effects on quality of life. In the US, compared with the general population, adults with a history of active epilepsy (i.e., with persisting seizures) are more likely to report fair or poor health, be unemployed or unable to work, live in households with the lowest annual incomes, and have a history of cooccurring medical disorders [10]. Adults with a history of epilepsy and with active epilepsy also tend to be obese, physically inactive, and currently smoking. Lower rates of marriage and fertility among people with epilepsy (even after adjustment for marriage) have been also reported [11]. Comparative findings from different European countries participating in a multicenter cohort study support the concept that epilepsy has a considerable impact on driving, education, occupation, leisure activities, and insurance [12]. The social implications of epilepsy in this sample are only partly related to its severity and clinical features. School achievement in children and adolescents with epilepsy is lower than in the general population and is independent of other neurological sources of impairment [13]. Children with epilepsy have very

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high rates of social problems in adulthood, even if they are neurologically and intellectually normal [1]. These problems persist even after remission of epilepsy and may require psychosocial support.

In turn, the economic and educational background of the society can have an influence on the disease itself and its comorbidities. In resource-poor countries, in the absence of appropriate healthcare services, the prevention, diagnosis, and care of epilepsy are problematic, resulting in increase in the incidence of the disease, the persistence of seizures, and even in higher premature mortality [14]. A number of preventable risk factors (perinatal disorders, infections and infestations, traumatic brain injuries) predominate, contributing to the higher burden of disease in these areas than in resource-rich countries. However, disparities in health management are also present in resource-rich countries and can be attributed to inequalities in healthcare that predominate, among others, in selected ethnicities, minorities, elders, immigrants and refugees, individuals with disabilities, and prisoners [15].

3. Epilepsy, cognitive impairment, and social functions

Psychosocial difficulties most frequently arise in people with epilepsy and cognitive impairment. Memory impairment, intellectual decline, reduced information processing speed, reduced reaction time, and attentional deficits are frequently reported in people with epilepsy [5]. Longer disease duration [16] and mesial temporal lobe involvement [17] are associated with an increased risk of cognitive impairment. Frequent seizures impair learning by reducing alertness and interfering with short-term information processing, storage, and abstraction [18]. Nocturnal seizures can disrupt the consolidation of memory [18]. In addition to seizures, interictal electroencephalographic (EEG) discharges can be implicated. Antiepileptic drugs can be also responsible as being frequently associated with learning difficulties, behavioral changes, and memory deficits [19]. These factors can have strong negative effects on educational achievement and occupational opportunities. Impaired cognitive functions, such as theory of mind (ToM), can have an impact on psychosocial well-being [20].

4. Social functions, site, and extent of epileptic activity

The involvement of psychosocial functions varies with side, site, and the severity of epileptic activity. Mesial temporal lobe epilepsy (MTLE) with hippocampal sclerosis tends to affect a number of cognitive functions, including learning, visuospatial functions, problem solving, memory, and academic achievement [21]. The impairment of the left hemisphere is predominant and is associated with a frequent defect in verbal memory [22] and word finding [23]. Cognitive impairment has been also shown to be more severe with left than right temporal lobe involvement [5]. Patients with frontal lobe epilepsy have been found to exhibit deficits in emotion recognition, ToM, and cognitive empathy, a function of orbitofrontal cortex [24]. Compared with MTLE, social cognition has been less frequently investigated in patients with idiopathic generalized epilepsies (IGE). However, studies in patients with mixed IGE found difficulties in emotion attribution tasks, higher-order social skills, irrespective of the specific syndrome [25]. Subtle brain structural alterations can be found in mesial prefrontal and temporoparietal cortex.

Temporal lobe abnormalities have been also implicated in the biological substrate of depression. In temporal lobe epilepsy, the degree of hippocampal atrophy is inversely associated with the severity and/or duration of depression [26]. Larger amygdala volumes have been observed in patients with temporal lobe epilepsy and psychosis [27]. Mood disorders have been also reported to be associated with widespread functional and anatomical abnormalities in the orbitofrontal cortex [28], cingulate gyrus [29,30], subcortical regions [29], and brainstem [30].

5. Social functions and age

Seizures in children interfere with the physiologic brain development altering normal development trajectories. Children and adolescents with epilepsy can have significant impairment in basic and higher-order cognitive functions, including facial emotion perception and ToM [31,32]. In a comprehensive review of the literature, Stewart and coworkers [33] summarized the available studies examining social cognition in pediatric epilepsies and found that the impairment of facial emotion perception and ToM did not differ across epilepsy phenotypes, suggesting that social cognitive impairment is a shared feature of epilepsy in childhood. In line with the International League Against Epilepsy (ILAE) concept that seizures arise from an altered network, a shared neural network has been postulated as the basis for social cognitive deficits. The same concept can be applied to adults, although in adult age, behavioral problems can have a multifactorial origin that results from the interaction between epilepsy-related factors and a number of social factors contributing to stigma. Social isolation and interpersonal problems are frequent findings in adults with epilepsy. The picture is even more complicated in the elderly. The aging process implies a variety of cellular changes with epileptogenic potential that include loss of dendritic spines, accumulation of inflammatory molecules, and deposition of beta amyloid and tau proteins [34,35]. These changes can have a profound impact on psychosocial functions making the attribution to a specific cause (among cognitive and intellectual status, social background, seizures, AEDs, psychiatric comorbidities, and stigma) difficult to disentangle from the other causes.

6. Psychiatric comorbidity in epilepsy

Psychiatric disorders are frequent comorbidities in people with epilepsy, with a lifetime history identified in up to one-third of children and adults [36]. Mood and anxiety disorders are the most frequent reports in the general population [37]. In children and adolescents, anxiety and depression have been documented in several clinical series [38,39]. Similar findings were observed in adults [37,40,41]. Psychiatric comorbidities have been documented even in specific epilepsy syndromes, including benign epilepsy with centrotemporal spikes [42], juvenile myoclonic epilepsy [43], and childhood absence epilepsy [44] that share a broad range of psychiatric, behavioral, and social problems. In children and adolescents, symptoms of anxiety have been found to be independent of the disease severity and duration and appeared to have negative consequences on the individuals and their families' quality of life [45].

A bidirectional relationship exists between epilepsy and depression. Common underlying pathophysiological mechanisms are a possible explanation. Data from epidemiologic studies and in animal models of depression and epilepsy support a potential role of pathogenic mechanisms of mood disorders in the development of epileptic seizures and epileptogenesis [46]. These findings add to the complexity of the interactions of different factors and their effects on social cognition.

7. Social implications of epilepsy and the public

Social maladjustment can be the consequence of stigma and reflect persisting negative attitudes of the public towards epilepsy. Misperceptions of epilepsy are still present in the general population. Although several studies indicate an increasing awareness of the disease, negative attitudes towards epilepsy are still reported in several developed and developing countries [47,48]. However, the negative attitudes tend to decrease with increasing education of the public. In Italy, a nationwide survey of knowledge and attitudes towards epilepsy showed increasing knowledge and better attitudes by the public when confronting the results with a previous nationwide interview [49]. However, a fairly high proportion of persons from the general population still exhibited misconceptions and posed strong limitations to daily living activities. In addition, awareness and attitudes varied significantly according to the

demographic and sociocultural characteristics of the interviewees. These observations are in line with several other reports from resource-rich and resource-poor countries [49] and provide the necessary background for continuing educational activities to remove inadequate knowledge and stigma about epilepsy.

8. Resilience and vulnerability in epilepsy

Epilepsy has been associated with social distress and vulnerability [50] and, consequently, poor quality of life. However, impairment of quality of life is strictly dependent on the complexity of the epilepsy phenotype, with special reference to the degree of seizure control [51]. Several other factors can be implicated, as above indicated. In a study in newly diagnosed patients [52], significant predictors of vulnerable outcome included, among others, the presence of depression and reduced sense of mastery. These and other factors can have strong negative effects on interpersonal relationships and contribute to social isolation.

9. The future

In May 2015, the World Health Assembly approved the WHO Resolution on the Global Burden of Epilepsy, a powerful tool to engage national governments in the implementation of effective actions to improve medical and social services for people with epilepsy, promote public awareness about epilepsy, and allocate resources to epilepsy research [53]. This resolution couples with the results of an ongoing global initiative aimed at assessing the burden of all diseases, injuries, and their complications (including epilepsy) whose findings have important implications for health service planning [54–57]. In that initiative, the burden of epilepsy is measured as deaths, prevalence, and disability-adjusted life-years (DALYs), a summary measure of health loss defined by premature mortality and persisting disability [58]. Between 1990 and 2016, there has been a nonsignificant change in the age-standardized prevalence of idiopathic epilepsy worldwide, but a significant decrease in age-standardized mortality and DALY rates. The decrease in death and DALY rates in patients with epilepsy is encouraging, but the changes varied across geographical areas and within countries and were linked to the sociodemographic development status. These findings should prompt more action in economically deprived areas. Thus, health service planners should be aware that patients with epilepsy are more often poor and marginalized because of stigma, requiring a greater effort to reach them than might be the case for most other diseases.

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