



## Introduction

## Investigating the social cognition phenotypes in children, adolescents, and adults with epilepsy

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## ABSTRACT

In recent years, clinical and neuropsychological assessment of patients with epilepsy has dedicated increasing attention to social cognition (SC), which is relevant to interpersonal relations, psychological well-being, and autonomy. The components of SC are supported by distinct but interlinked brain regions that may be affected by focal and generalized epilepsy. This special issue sought to describe some of the societal, clinical, and pathophysiological correlates of SC in patients with epilepsy and healthy subjects, highlighting some of the questions key to clinical care and research.

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## 1. Introduction

A wide range of neurobehavioral disorders including cognitive, psychopathological, and social-adaptive problems may affect the patient with epilepsy, sometimes preceding seizure onset and often persisting after seizure control. These disorders may be life-long, increasing use of healthcare resources, and limiting education and employment engagement. Within this framework, social cognition (SC) has become a more and more relevant aspect of the cognitive phenotypes associated with epilepsy.

The social functions extend to multiple aspects of life, such as contact and connection between individuals, cooperation, communication, and sense of belonging, all of which relate to the functioning of brain networks [1,2]. Satisfactory social functioning substantially contributes to mental and physical health and socioeconomic autonomy, while social isolation and loneliness can accentuate frailty and risk of disability [3–5].

Social cognition is a higher-order cognitive domain that allows one to construct the mental representations of interpersonal relationships and to use them flexibly in social contexts. Integrated cognitive models describe distinct components of SC such as theory of mind (ToM), empathy, emotion processing, appreciation of interpersonal relationships, and moral judgment [6,7]. In 2013, the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-5) introduced SC as one of six core components of neurocognitive function [8]. In 2007, Hermann et al. [9] proposed the phenotypic approach to the study of

cognition and behavior in patients with epilepsy, emphasizing memory impairment as an isolated feature or in combination with other cognitive defects. The study of SC may arguably extend such a perspective, representing a bridge between cognitive impairment, psychological well-being, and interpersonal behavior.

This special issue of *Epilepsy & Behavior* sought to address aspects of SC linked to epilepsy, stimulating the attention on this as yet relatively sparsely investigated feature of the cognitive profile of patients with epilepsy. The papers included in the issue present both new experimental and review data on SC and related cognitive functions in children, adolescents, and adults with epilepsy and healthy subjects, encompassing patterns and the pathophysiological correlates of impairment, as well as psychopathology, societal features, and quality of life (QoL).

## 2. Children

In children and adolescents with epilepsy, as outlined by F.M.C. Besag and M.J. Vasey, SC has been less frequently and less comprehensively assessed than in adult patients. Specific neuropsychological evaluations have been conducted in selected populations with epilepsy associated with neuropsychiatric disorders known to affect SC, such as autism spectrum disorder and attention-deficit hyperactivity disorder. Within this framework, children and adolescents with West syndrome, Dravet syndrome, Landau–Kleffner syndrome, or juvenile myoclonic epilepsy show impaired SC. Persistence of various impairments of SC after seizure control can impact on patients' QoL, but early management of these problems can help prevent or attenuate long-term negative effects.

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E. Stewart, S. Lah, and M.L. Smith reviewed the literature on facial emotion perception (FEP) and ToM in children and adolescents, reporting very similar impairments in children with generalized or focal epilepsies and in children with different sites of the epileptic zone. While ToM is linked to social competence, there is no evidence of an association between FEP and measures of social functioning. Interestingly, as in adult patients [10], out of the epilepsy-related variables, only seizure frequency and disease duration affect FEP and ToM.

E. Stewart, C. Catroppa, and colleagues present new experimental data in children aged 8 to 16 years with genetic generalized epilepsy (GGE) or temporal lobe epilepsy (TLE), demonstrating that FEP is significantly impaired in comparison with healthy children. Moreover, distinct emotions appear to be compromised in GGE and TLE, suggesting that neurodevelopment may influence the perception of single emotions. Social competence was also altered in both groups but it bore no relationship to FEP.

### 3. Adults

A.R. Giovagnoli analyzed the epistemic and affective components of ToM in healthy adults from age 16 to age 81 years, showing that ToM is a specific cognitive domain independent of age and formal education. In contrast, some ToM processes have been related to sex, executive functions, and reality examination. The findings derived from the neuropsychological assessment in healthy subjects may provide reference points for clarifying the SC phenotype in patients with epilepsy.

The study of SC in patients with epilepsy is also supported by knowledge of the normal neurophysiological processes in healthy subjects. F. Panzica and colleagues, using an experimental electroencephalographic (EEG) model in healthy adults, found that ToM processes are associated with immediate specific changes of brain connectivity, as expressed by high cortical coherence in the gamma band in the right frontal and parietal areas. Further study of EEG coherence may help determine the neural dysfunctions associated with impaired ToM in patients with epilepsy.

Across the lifespan, in patients with epilepsy, social function and SC may be impaired as a consequence of neurodevelopmental alterations, seizure-related factors (including the effects of antiepileptic drugs (AED)), stigma, and psychiatric comorbidities. As reported by E. Beghi, an interplay between these features and personal variables may interact to cause different types of SC disorders.

M. Jogarajah and M. Mula discuss the results of studies concerning the impact of SC on QoL. There is evidence that impaired SC and ToM can affect QoL independently of seizure-related factors, mood, and general cognitive functioning. Current findings need to be replicated, aiming to contribute to diagnosis and treatment of impaired SC.

While many studies have addressed SC in adults with focal epilepsies, less attention has been given to idiopathic generalized epilepsies (IGE). M. Guida and colleagues underline that few studies in groups with mixed IGE have reported inconsistent results pertaining to emotion attribution, while other investigations have highlighted more consistently found defects of ToM. Subtle abnormalities in the mesial frontal lobe and in the temporoparietal cortex, as well as impaired executive functions, have been identified as pathogenic mechanisms.

### 4. Conclusions

Current findings in adults and children with epilepsy are integrated with the results of previous studies on SC in epilepsy. Children and adult patients with TLE or GGE consistently appear at risk of impairment of ToM and FEP, dependent of the age at seizure onset, disease duration, and seizure frequency. Across the lifespan, SC, in particular ToM, may be distinct from other cognitive domains, which may be linked to different brain connectivity patterns. Impaired ToM may impact on the QoL and social competence at different ages.

In this scenario, there are numerous directions that may guide clinical care and future research. At the clinical level, cross-national investigations of SC in patients with epilepsy and healthy controls could delineate the developmental course of SC from childhood to the elderly and its determinants and pathogenic mechanisms.

Standardized repeatable neuropsychological batteries are needed to assess not only ToM but also the various components of SC, providing culture-related normative data.

The impact of frontal lobe epilepsy and GGE in adult and children patients deserves further studies and comparisons with the larger research body on SC of TLE, contributing to the characterization of SC in different epilepsy disorders.

An important issue is the complex interaction between SC, psychosocial functioning, and QoL, which, at any age, can affect a patient's autonomy and health.

The planning of nonpharmacological treatments, paralleling AED therapy or surgical interventions, and assessment of their effectiveness using randomized controlled studies, as suggested by different authors, represent an important line of clinical research.

### Declaration of Competing Interest

The authors have no conflict of interests.

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