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Review

Patterns of impaired social cognition in children and adolescents with epilepsy: The borders between different epilepsy phenotypes

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ABSTRACT

Over the past decade, a growing number of studies have shown that children and adolescents with focal and generalized epilepsies have marked impairments in social cognition, including deficits in facial emotion perception (FEP) and Theory of Mind (ToM). At present, it remains unclear whether FEP and ToM impairments are comparable in children with focal and generalized epilepsies or whether distinct syndrome-specific deficits have emerged. This question of whether unique or overlapping social cognitive profiles exist in epilepsy is of interest, given that the revised International League Against Epilepsy (ILAE) classification guidelines propose that seizures arise from a diseased network (i.e., network account), rather than being confined to discrete regions near the site of seizure foci (i.e., localization account). The purpose of this review was as follows: (1) to summarize studies examining FEP and ToM in pediatric patients with epilepsy, (2) to examine epilepsy and psychosocial correlates of these difficulties, and (3) to determine whether patterns of sociocognitive impairment better support a localization or neural network account of epilepsy. Twelve studies were reviewed examining FEP (N = 5) and/or ToM (N = 8). Findings revealed significant FEP and ToM impairments across the studied subgroups with epilepsy, which did not differ between children with generalized and focal (localization-related) epilepsies nor among children with different subtypes of localization-related epilepsy. Similarly, other epilepsy variables (i.e., seizure frequency, side of seizure focus, number of antiepileptic drugs (AEDs) or surgical status) were not related to FEP or ToM, with the exception of younger age at seizure onset and longer duration of epilepsy. Several studies documented a significant relationship between impaired ToM and reduced social competence in pediatric patients with epilepsy, whereas evidence for a relationship between FEP and psychosocial functioning is currently weak. In conclusion, findings suggest that social cognitive impairments represent a shared feature of epilepsy in childhood. The results support a neural network account of epilepsy, in which a shared neural network of dysfunction may be underlying social cognitive deficits in this group. Further research is needed to examine the functional correlates of social cognitive impairments, as well as to evaluate screening tools and treatment methods to identify and address significant social and emotional difficulties in this patient group.

This article is part of the Special Issue "Epilepsy and social cognition across the lifespan".

1. Introduction

Social cognition refers to the ability to understand, interpret, and respond appropriately to social and emotional cues of others [1]. It encompasses basic emotion perception and decoding abilities (e.g., facial emotion perception [FEP], prosody perception) as well as higher-order skills that enable children to infer thoughts, intentions, beliefs, and emotions of others and themselves, and/or to act on this mental state knowledge in sensitive and socially appropriate ways (e.g., Theory of Mind [ToM], empathy, moral reasoning) [2]. These social cognitive processes function rapidly and in parallel, allowing individuals to understand and interpret social–emotional information, such as facial expressions, prosody, eye-gaze, and implicit meanings in action and speech [1]. As such, social cognition is crucial for adaptive interpersonal functioning in both children and adults.

Neuroimaging and lesion studies have implicated a network of brain regions in the temporal and frontal lobes in the development of social cognition, including the medial prefrontal frontal cortex (mPFC), anterior cingulate cortex (ACC), superior temporal sulcus (STS), temporoparietal junction (TPJ), temporal poles, and the

Abbreviations: CBCL, Child Behavior Checklist; FEP, facial emotion perception; POFA, pictures of facial affect task; RMET, reading the mind in the eyes tasks; ToM, Theory of Mind.

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amygdala [2,3]. Within this network, overlapping and discrete neural regions have been implicated in basic and higher-order social cognitive skills. For instance, FEP and ToM have both been associated with activation and integrity of the mPFC and STS [4–6]. In addition, FEP has been uniquely associated with frontal operculum, right amygdala, and orbitofrontal cortex activation [6–8] whereas ToM has been associated with activation and integrity of the TPJ, anterior frontal poles, dorsolateral and ventromedial prefrontal cortex, and bilateral temporal poles [4,9]. In patients with epilepsy, disruption to core parts of this network as a result of seizures and/or focal lesions or pathology could impair social cognitive skills. The pattern of social cognitive impairment expected to occur depends on how epilepsy and seizures are classified and defined; specifically, whether seizures are viewed as arising from and affecting (i) discrete localized brain regions (i.e., localization account) or (ii) a diseased network in which overlapping cortical and subcortical structures may be affected, regardless of whether seizures emanate from a specific focal site (i.e., neural network account) [10].

From a localization account of epilepsy, children with focal seizures emanating from core parts of the sociocognitive network (i.e., temporal lobe epilepsy (TLE), frontal lobe epilepsy (FLE)) might be expected to present with significantly larger social cognitive impairments than children without localized lesions/pathology to these regions of the brain (i.e., genetic generalized epilepsy (GGE)). In contrast, from a network account, in which focal and generalized seizures are presumed to arise from a diseased network [11], children with focal and generalized epilepsies might be expected to present with largely comparable social cognitive impairments given the expectation of dispersed and overlapping neural dysfunction across subgroups with epilepsy [10]. This network account has arisen from the revised phenomenological approach to classifying epilepsies and seizures, which was put forward by the ILAE Commission on Classification and Terminology (2005–2009) [11]. This revised approach has provided a fundamental shift in the way cognition and behavior are viewed in epilepsy [10] and has been used to explain shared patterns of cognitive impairment in other domains (e.g., memory, executive functions) among pediatric patients with epilepsy [12] but has not yet been applied to studies examining social cognition.

Over the past decade, a growing number of studies have shown that children and adolescents with epilepsy have significant impairments in both basic and higher-order social cognition, including FEP [13,14] and ToM [15,16]. These impairments have been found among children and adolescents with focal epilepsies [17,18], including TLE [13,19], FLE [13], and benign epilepsy in childhood with centrotemporal spikes (BECTS), as well as among children with GGE [14,16]. These findings suggest that social cognitive deficits may represent a shared feature of epilepsy in childhood; however, a comprehensive review of the literature examining both basic and higher-order social cognition in children and adolescents with epilepsy is yet to be carried out. As such, it remains unclear whether the magnitude and pattern of social cognitive impairment are shared across epilepsy subtypes or whether distinct, syndrome-specific deficits have emerged.

The purpose of this paper was to review the literature on social cognition in children and adolescents with epilepsy, focusing on FEP and ToM, as two core social cognitive skills that have been studied in pediatric patients with epilepsy thus far. In doing so, the review will provide a platform to examine whether patterns of sociocognitive impairments provide greater support for a localization or neural network account of epilepsy. In addition, this manuscript will examine whether sociocognitive impairments differ as a function of basic demographic and cognitive skills (i.e., sex, intellectual functioning), and whether they are related to epilepsy variables or psychosocial functioning. These analyses may provide clinically useful information for detecting and treating social cognitive deficits in this patient group.

2. Facial emotion perception

Facial emotion perception is the ability to accurately identify and label emotional expressions on faces, with six universally identifiable emotions recognized by humans: happiness, sadness, anger, fear, disgust, and surprise [20,21]. The ability to recognize and label these six emotions, along with neutral facial expressions, develops gradually throughout childhood and has been most widely assessed with tasks that require participants to select an emotion label that best depicts a target face [22].

Table 1 summarizes studies examining FEP in children and adolescents with epilepsy. All studies have found significant overall FEP impairments, meaning across basic facial emotions assessed, in patients with epilepsy compared with typically developing controls, including among groups with focal (i.e., FLE, TLE and/or extra-TLE/FLE) [13,18,19] and generalized (i.e., GGE) [14] epilepsy. Only one published study has compared FEP as a function of subtypes of localization-related epilepsy; this study found no significant differences between children and adolescents with TLE and FLE in overall FEP accuracy [13]. In addition to these published papers, we recently conducted a cross-sectional study examining and comparing FEP in children and adolescents with TLE and GGE [27]. Similar to Golouboff et al. [13], we found overall FEP impairments in children and adolescents with GGE and TLE relative to controls, but no significant differences between the two groups with epilepsy. These findings are consistent with the adult literature, in which a recent meta-analysis found significant facial emotion recognition deficits in adults with TLE, FLE, GGE, and unspecified epilepsies (i.e., independently in each group), and no significant differences in FEP performance between these subgroups with epilepsy [28].

Despite the consistency of results discussed so far, when accuracy at identifying specific facial emotions has been examined, findings have been mixed. One study found that children who had undergone focal epilepsy resections of the temporal, frontal, or extratemporal/frontal lobes were impaired in recognizing sadness, disgust, and surprise, but not happiness, anger, or fear, compared with controls [18]. Pinabiaux et al. [19] also examined children following epilepsy surgery (temporal lobe resection only) and found evidence for a discrete reduction in fear recognition. However, this study only assessed recognition of three basic facial emotions (fear, happiness, neutral) and did not statistically compare the performance of the group with TLE with healthy controls, but used a cut-off score to classify children as with impairments or without impairments [19]. A third study that included a mixture of pre- and postsurgical children found impairments in fear and neutrality among children with left-sided TLE, disgust among children with right-sided TLE, and happiness among children with FLE, when compared with controls [13]. The fourth study found impairments in all basic facial emotions among adolescents with GGE, including happiness, sadness, anger, fear, disgust, and surprise [14]. In a recent study, emotion-specific impairments in groups with GGE and TLE were further at odds with this published literature: children and adolescents with GGE were impaired in recognizing anger and disgust whereas the group with TLE were impaired in sadness and disgust compared with controls [27].

Although different patterns of emotion-specific impairments documented in past studies could reflect real differences between subgroups with epilepsy, it is also possible that inconsistencies relate to methodological factors, such as differing sample sizes and lack of sensitivity of the FEP tasks used. All studies have used variations of the same validated FEP task, which present the six basic facial emotions at maximum intensity. These tasks are relatively blunt compared with newer FEP batteries that present facial emotions of graded valences (e.g., 75%, 50%, 25% intensity) [29,30]. Thus, lack of significant differences between groups with epilepsy and control for certain emotions may not reflect a lack of impairment but rather a lack of sensitivity of tasks used. Another possible explanation is that different patterns of impairment relate to differing epilepsy or demographic characteristics

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Table 1
Characteristics of studies examining social cognition in children and adolescents with epilepsy.

Study	Sample characteristics (age and IQ, means ± SD or range)	Epilepsy characteristics	Social cognitive domain: task	Results
Braams et al. [18]	Focal epilepsy[a] $N = 41$ (24 girls), mean age = 13.5 ± 4.4 years, VIQ = 84 ± 19.9 HC $N = 82$ (48 girls), age = 13.5 ± 4.4 years, VIQ = 113 ± 15.1	Age at seizure onset (mean: 5.0 ± 4.2 years), side of seizure focus (25 left, 16 right), all postsurgery with amygdala resected ($N = 15$) or amygdala in situ ($N = 26$)	FEP: POFA (happiness, sadness, fear, disgust, anger, surprise)	Focal epilepsy < HC for FEP (total score, sadness, disgust, and surprise) Total FEP accuracy significantly related to VIQ. Total FEP accuracy not significantly related to sex. Longitudinal analysis of a subset of children ($N = 11$) presurgery and 2 years postoperatively found no change in FEP
Genizi et al. [23]	BECTS $N = 15$ (sex not reported), mean age = 10.53 ± 2.21, IQ not reported. HC $N = 15$ (sex not reported), mean age = 10.40 ± 1.06, IQ not reported.	Age at seizure onset (mean: 7.6, range: 5 to 12 years)	ToM: False belief ('Yoni task' measuring cognitive and affective ToM)	BECTS < HC on affective ToM but not cognitive ToM Within BECTS, affective ToM < cognitive ToM
Golouboff et al. [13]	FLE $N = 8$ (5 girls), mean age = 12.60 ± 2.70, VIQ = 105 ± 18 TLE $N = 29$ (13 girls), mean age = 13.30 ± 2.90, VIQ = 97 ± 13 HC $N = 37$ (not reported)	FLE, age at seizure onset (mean: 5.8 ± 2.6 years), side and surgery not reported. TLE, age at seizure onset (5.4 ± 3.9), side of seizure focus (16 left, 13 right), surgery (14 presurgery, 15 postsurgery).	FEP: TREFE (happiness, sadness, fear, disgust, anger, neutrality)	FLE < HC for FEP (happiness only) LTLE < HC for FEP (total score, fear, and neutrality) RTLE < HC for FEP (disgust only) Overall group with TLE not compared with HC Younger age at seizure onset correlated with worse total FEP accuracy in children with TLE
Jiang et al. [14]	GGE $N = 42$ (15 girls), mean age = 14.0–19.5, IQ from MoCA = 26–28.5/30 HC $N = 47$ (18 girls), mean age = 15.0–19.0, IQ from MoCA = 27–29/30	Age at seizure onset (mean: 12.0, range: 10–15 years)	FEP: EBEDT (happiness, sadness, anger, fear, disgust, and surprise) ToM: ECEDT (comparable with RMET)	GGE < HC for FEP: happiness, sadness, anger, fear, disgust, and surprise GGE < HC for ToM
Lew et al. [17]	GGE $N = 20$ (12 girls), mean age = 11.5 ± 2.5, FSIQ = 95.1 ± 16.8 Focal epilepsy[a] $N = 27$ (15 girls), mean age = 11.7 ± 2.2, FSIQ = 87.5 ± 14.1 HC $N = 57$ (29 girls), mean age = 11.7 ± 2.3, FSIQ = 104.5 ± 12.8	GGE, age at seizure onset (mean: 7.2 ± 2.9 years). Focal epilepsy, age at seizure onset (mean: 6.8 ± 2.8 years), side of foci and surgical status not reported.	ToM: Strange stories and RMET	GGE < HC on strange stories but not RMET Focal epilepsy < HC on strange stories but not RMET GGE = focal epilepsy on strange stories and RMET FSIQ significantly related to ToM (strange stories) when epilepsy and controls pooled; relationship not reported for independent groups.
Lunn et al. [24]	Epilepsy unspecified type $N = 56$ (sex not reported), mean age = 11.1 ± 2.3, FSIQ = 60–121 HC $N = 62$ (sex not reported), mean age = 10.5 ± 2.6, FSIQ = 83–121	Age at seizure onset (mean: 5.7 ± 2.9 years)	ToM: Strange stories and RMET	Epilepsy < HC on strange stories and RMET Younger age at seizure onset correlated with reduced ToM on strange stories
Pinabiaux et al. [19]	TLE $N = 25$ (7 girls), mean age = 13.1 ± 3.7, VIQ = 70–112 HC $N = 15$ (7 girls), mean age = 13.5 ± 3.4, IQ not reported.	Age at seizure onset (mean: 3.02 ± 2.4 years), side of seizure focus (12 left, 13 right), all postsurgery.	FEP: TREFE (happiness, fear, neutrality)	TLE < HC for FEP (fear only) LTLE = RTLE for FEP (total score, happiness, fear, and neutrality) Younger age at seizure onset correlated with poorer fear recognition
Raud et al. [25]	Focal epilepsy[a] $N = 25$ (20 girls), mean age = 10.4 ± 1.8, IQ not reported. GGE $N = 10$ (16 girls), mean age = 10.6 ± 2.0, IQ not reported. HC $N = 30$ (10.3 ± 1.9)	Focal epilepsy, age at seizure onset (mean: 9.1 ± 2.0 years). GGE, age at seizure onset (mean: 9.2 ± 2.3 years).	ToM: Advanced ToM story task	Epilepsy < HC for ToM Within the group with epilepsy, GGE < focal epilepsy for sarcasm stories but no other story types Earlier onset of seizures correlated with reduced ToM
Stewart et al. [16]	GGE $N = 22$ (14 girls), mean age = 12.8 ± 2.8, FSIQ = 90.96 ± 10.27 HC $N = 22$ (12 girls), mean age = 12.4 ± 2.5, FSIQ = 111.41 ± 13.76	Age at seizure onset (mean: 6.4 ± 3.6 years).	ToM: Strange stories and faux pas	GGE < HC on strange stores and faux pas tasks Within the group with GGE, affective ToM < cognitive ToM Higher daily dosage of sodium valproate correlated with poorer affective ToM task
Stewart et al. [26]	TLE, $N = 22$ (11 girls), mean age = 13.9 ± 2.2, VIQ = 93.59 ± 9.18 HC $N = 22$, (12 girls), mean age = 12.4 ± 2.5, VIQ = 111.41 ± 13.76	TLE, age at seizure onset (mean: 7.9 ± 4.6 years), side of seizure focus (14 left, 8 right), surgical status (10 postsurgery, 12 presurgery).	ToM: Strange stories and faux pas	TLE < HC on strange stores and faux pas tasks Younger age at seizure onset and longer duration of epilepsy correlated with poorer ToM on strange stories task VIQ not significantly related to ToM in group with TLE.

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Table 1 (*continued*)

Study	Sample characteristics (age and IQ, means ± SD or range)	Epilepsy characteristics	Social cognitive domain: task	Results
Stewart et al. [27]	GGE $N = 22$ (14 girls), mean age = 12.8 ± 2.8, FSIQ = 90.96 ± 10.27 TLE $N = 22$ (11 girls), mean age = 13.9 ± 2.2, FSIQ = 101.05 ± 11.04 HC $N = 22$ (12 girls), mean age = 12.4 ± 2.5, FSIQ = 111.41 ± 13.76	GGE, age at seizure onset (mean: 6.4 ± 3.6 years). TLE, age at seizure onset (mean: 7.9 ± 4.6 years), side of seizure focus (14 left, 8 right), surgical status (10 postsurgery, 12 presurgery).	FEP: POFA (happiness, sadness, fear, disgust, anger, neutrality)	GGE < HC for FEP (total emotions, anger, and disgust) TLE < HC for FEP (total emotions, sadness, and disgust) GGE = TLE for FEP (total score and for each emotion examined) LTLE = RTLE for FEP (total score and for each emotion examined) Presurgery = postsurgery for FEP (total score and for each emotion examined)
Zhang et al. [15]	GGE $N = 54$ (17 girls), mean age = 11.9 ± 1.6, IQ not reported HC $N = 37$ (12 girls), mean age = 11.46 ± 1.0, IQ not reported	GGE, age at seizure onset (mean: 8.8 ± 2.7 years).	ToM: False belief and faux pas	GGE < HC on false belief and faux pas tasks Sex not related to ToM in group with GGE. Longer duration of epilepsy correlated with poorer ToM on both tasks

BECTS, benign epilepsy in childhood with centrotemporal spikes; EBEDT, eyes basic emotion discrimination task (equivalent to POFA); ECEDT, eyes complex emotion discrimination task (equivalent to RMET); extra-TLE/FLE, extratemporal/frontal lobe epilepsy; FEP, facial emotion perception; FLE, frontal lobe epilepsy; GGE, genetic generalized epilepsy; HC, healthy control; MoCA, Montreal Cognitive Assessment; RMET: reading the mind in the eyes task; POFA, pictures of facial affect task; TREFE, test de reconnaissance des emotions faciales (French task that parallels the POFA); TLE, temporal lobe epilepsy; ToM, Theory of Mind; FSIQ, Full Scale IQ; LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; SD, Standard deviation; VIQ, Verbal IQ.

[a] Groups with focal epilepsy included a mixture of TLE, FLE, and extra-TLE/FLE.

of participant groups. For instance, age at testing could affect whether significant differences are observed between groups with epilepsy and control, as the ability to recognize different facial emotions emerges gradually throughout childhood. If typically developing controls have not acquired the capacity to identify certain emotions at the time of testing, then it is unlikely that differences between groups will emerge. Recent neuroimaging findings also do not support the idea that children with different epilepsy subtypes would be impaired in recognizing some facial emotions, but not others. Although early research from adults suggested that specific brain regions were implicated in processing certain emotions, such as the amygdala in fear [31], two recent meta-analyses of neuroimaging studies found little evidence that discrete emotions could be consistently localized to distinct brain regions [32,33]. Rather, accuracy at recognizing facial emotions was associated with overlapping and interacting cortical networks, which allowed for plasticity of function in childhood [33]. These findings suggest that seizures and/or pathology to central or peripheral networks implicated in FEP are likely to interfere with recognition a range of different facial emotions.

Finally, in typically developing children, sex and intellectual quotient (IQ) have been found to relate to FEP, with a consistent advantage documented among girls [34,35] and children with higher verbal IQ [36]. Only one study examined sex differences in children with epilepsy, and this study found no significant differences between boys and girls in FEP accuracy [18]. This same study also examined the relationships between IQ and FEP; similar to prior findings from typically developing children [36], the authors found a significant relationship between verbal IQ and FEP in both groups with focal epilepsy and control [18]. Despite this relationship, FEP impairments were still apparent in children with epilepsy relative to controls while controlling for verbal IQ. Further research would help to clarify whether verbal and/or performance IQ are related to FEP in children with different epilepsy subtypes, as well as to reexamine sex differences in FEP.

Overall, the current findings suggest that FEP impairment represents a shared feature of epilepsy in childhood. At present, the pattern of emotion specific impairments is not clear, and further research with more fine-grained FEP batteries could help to clarify results.

3. Theory of Mind

Theory of Mind refers to the ability to understand the thoughts, intentions, beliefs, and emotions of oneself and others [37]. It encompasses component processes, including the capacity to understand mental states, such as knowledge and beliefs (i.e., cognitive ToM) as well as emotional states (i.e., affective ToM). Theory of Mind develops gradually throughout childhood, first emerging with a basic understanding of beliefs and extending to more advanced understandings of both cognitive and affective states. Early emerging (i.e., elementary) ToM has been most widely assessed with false belief tasks [38] whereas later developing (i.e., advanced) ToM has been assessed with various paradigms that require children to infer emotional states based on eye-gaze expression (e.g., reading the mind in the eyes tasks [RMET]) or to understand thoughts and feelings of characters in stories (e.g., strange stories, faux pas task) [39].

Theory of Mind impairments have been documented in children and adolescents with both generalized [15–17] and focal [17,26] epilepsies on elementary [23] and advanced [14,16,17,24] ToM tasks (Table 1). The most consistent impairments have been documented on advanced ToM story tasks [25], such as the strange stories [16,17,24] and faux pas [15,16] tasks, which require children to explain social scenarios containing nonliteral or implicit meanings such as white lies, sarcasm, metaphors, and social faux pas. Theory of Mind impairments have also been documented on false belief tasks [15,23] and on the RMET in two studies [14,24], but not a third study [17]. To date, only two published studies have compared ToM performance in children and adolescents with different epilepsy types [17,25]. Lew et al. [17] found no significant differences in ToM between children with GGE and focal epilepsies (TLE, FLE, and extra-TLE/FLE) on two advanced ToM tasks: strange stories task and RMET. Similarly, Raud et al. [25] found comparable overall ToM performance among children with generalized and focal epilepsies on an advanced ToM story task. In this study, a discrete difference between groups with epilepsy was found when performance for specific story types was examined: children with generalized epilepsy had greater difficulty answering questions in stories containing sarcasm than did children with focal epilepsy, although this difference was based on responses to just two stories [17].

In addition to overall ToM deficits, three studies have examined within-group differences in cognitive and affective ToM; all of these studies found significantly larger impairments in affective relative to cognitive ToM in children and adolescents with GGE, TLE, and BECTS [16,23,26]. However, whereas two studies [16,26] found that children with GGE and TLE were impaired in both cognitive and affective ToM relative to controls, the third study [23] found a discrete impairment in affective ToM among children with BECTS. The lack of significant

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impairment in cognitive ToM in Genizi et al.'s [23] study may relate to (i) the use of an elementary ToM task (false belief) that may lack sensitivity to ToM deficits in children aged 7 to 13 years who participated in this study or (ii) the small number ($N = 15$) of children with epilepsy assessed, which limited statistical power. The two other studies used an advanced ToM task (faux pas) and assessed 44 children with GGE and TLE ($N = 22$ in each group) [16,26]. The combination of a more difficult task and larger sample size may have resulted in a statistically significant difference between groups for cognitive ToM.

Similar to FEP, a female advantage has been documented in ToM among typically developing children [40,41], yet the only study to examine sex differences in FEP in children with epilepsy found no significant differences between boys and girls on an elementary (i.e., false belief) or advanced (i.e., faux pas) ToM task [15]. With respect to general cognitive skills, relationships between IQ and ToM in the general population have been mixed; some studies have found that both verbal and performance IQ related to ToM in typically developing children [42] and children with neurodevelopmental conditions [43,44] whereas another study found no significant relationship between either IQ domain and ToM [45]. Findings for children with epilepsy have also been mixed. Stewart et al. [26] found no significant relationship between verbal IQ and ToM (strange stories or faux pas) in children with TLE whereas Lew et al. [17] found that full scale IQ was significantly related to ToM (strange stories) in a pooled group with epilepsy and control. Finally, Lunn et al. [24] dichotomized children with epilepsy into those with low IQ (full scale IQ < 80) and higher IQ (full scale IQ > 80). They found that children with lower IQ performed significantly worse than children with higher IQ on the RMET and strange stories task; however, both groups (low and high IQ) performed significantly below controls [24]. Irrespective of the relationship between IQ and ToM, studies have found that children with epilepsy still have significant ToM impairments relative to controls while controlling for IQ [26,46]. These findings suggest that ToM impairments are not solely attributable to IQ in children with epilepsy but also highlight the need for further research to examine whether there is a significant relationship between IQ and ToM in pediatric patients with epilepsy.

Together, the current findings suggest that children with epilepsy have marked ToM impairments, which seem to be particularly pronounced in the emotional reasoning aspects of ToM. Similar to FEP, ToM impairments appear to represent a common feature in children and adolescents with epilepsy.

4. Relationship between facial emotion perception and Theory of Mind

The findings reviewed so far demonstrate significant impairments in both FEP and ToM in children and adolescents with epilepsy. Somewhat surprisingly, however, no significant relationship has been documented between these sociocognitive skills. Only one study has examined multiple social cognitive skills in children with epilepsy; this study found that adolescents with GGE were impaired in both FEP and ToM, yet there was no significant relationship between these deficient skills [14]. Similarly, several studies of adults with epilepsy have found significant impairments in FEP and ToM in patients with TLE [47,48], FLE [49], and extra-TLE/FLE [47] yet deficits in these skills have not been significantly related to each other. In a recent study of children and adolescents with autism spectrum disorder (ASD), ToM and FEP impairments were also present but not related to one another [50]. Taken together, these findings suggest that while FEP and ToM may be concurrently impaired in children with epilepsy and other neurodevelopmental conditions, they seem to be dissociable skills in these patient groups.

To further understand the relationships between various domains of social cognition, it may be useful to consider relationships between various subcomponents of FEP and ToM. The ability to identify and label faces expressing different emotions (e.g., anger, disgust, sadness) has been found to be correlated in children with [27] and without [51] epilepsy, and neuroimaging evidence has shown that an overlapping cortical network is implicated in identifying a variety of emotions [33]. Cognitive and affective ToM have also been found to show a significant relationship to one another in children with epilepsy [26] and in healthy controls [52]. However, unlike FEP, there is stronger evidence to suggest that cognitive and affective ToM are at least partly dissociable skills that rely on distinct neural networks [52,53], and that affective ToM is a more complex skill that requires multiple inputs [53], which may explain why children with epilepsy have more severe impairments in affective than in cognitive ToM.

A neurocognitive model of cognitive and affective ToM (and empathy) put forward by Shamay-Tsoory et al. [54] proposes a relationship between these components of ToM. The model hypothesizes the following: (1) cognitive ToM is a prerequisite for affective ToM and (2) affective ToM relies not only on cognitive ToM but also emotional contagion or the ability to feel another person's distress. These two inputs involve different neurocognitive processes: cognitive ToM involves conscious processing in order to bring to mind and verbalize thoughts and feelings whereas emotional contagion may bypass conscious thought processes through the functioning of the mirror neuron system [55]. In another preliminary model proposed to explain sociocognitive impairments in children with traumatic brain injury, Dennis et al. [56] similarly hypothesized that distinct neural systems were involved in cognitive ToM, affective ToM, and empathy. The mentalizing network, which involves functioning of the prefrontal cortex, STS, TPJ, and temporal poles, is said to enable individuals to understand both thoughts and feelings (cognitive and affective ToM) at a conscious cognitive level [56]. The mirror neuron empathy network, on the other hand, involves firing of neurons in the central premotor area, inferior parietal lobule, and inferior frontal gyrus and is important for affective ToM and empathetic responding [56]. In both of these models, affective ToM is proposed to rely on functioning on two complimentary neural pathways. In children with epilepsy, affective ToM may be more sensitive to disruption as it relies on a more widespread neural network than cognitive ToM and may be compromised by disruption to one or both neural networks. In addition, because cognitive ToM is a precursor to affective ToM, there may not only be an impairment but also a delay in affective skills emerging.

The model proposed by Shamay-Tsoory et al. [54] also proposes a relationship between ToM and empathy. To date, however, only one study has examined empathy, alongside ToM and FEP, in pediatric patients with epilepsy [14]. This study used a self-report scale (the Interpersonal Reactivity Index [57]) to examine empathy in adolescents (13 to 19 years old) with GGE [14]. The authors found significant impairments in FEP, ToM, and cognitive empathy but not affective empathy in the group with GGE [14]. In addition, they found that both FEP and ToM were significantly related to cognitive empathy whereas FEP and ToM were not related to each another. Cognitive empathy is broadly synonymous with cognitive and affective ToM in that it involves a conscious verbal understanding of thoughts and feelings and has been found to engage the same mentalizing network as ToM, i.e., the mPFC, TPJ, and STS [58]. Affective empathy, on the other hand, is said to rely more on the functioning of the mirror neuron system and involves an emotional contagion response [58,59]. This preliminary dissociation between cognitive and affective empathy observed in adolescents with GGE is intriguing yet difficult to explain given the literature is so limited. Further studies with larger and more heterogeneous groups with epilepsy are needed to examine empathy and its relationship to both ToM and FEP.

5. Epilepsy variables and social cognition

Relationships between seizure variables (i.e., age at seizure onset, duration of epilepsy, seizure frequency, seizure laterality) and treatment factors (i.e., surgery, antiepileptic drugs [AEDs]) with FEP and ToM have been examined in a number of prior studies, with significant

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findings reported for some variables but not others. Younger age at seizure onset has been related to reduced FEP in children with TLE [13,19] and to poorer ToM in children with unspecified epilepsy types [24] while longer duration of epilepsy has been related to reduced ToM in children and adolescents with GGE [15]. Seizure frequency has not been related to either ToM or FEP in any prior studies [13,16,19,24].

With respect to seizure laterality, two studies found no significant differences in overall FEP accuracy between children with left TLE and right TLE [13,19]. Pinabiaux et al. [19] also found no differences between groups for specific emotions (i.e., fear, happiness, or neutrality) whereas Golouboff et al. [13] found that children with left TLE had significantly larger impairments recognizing fearful faces compared with children with right TLE. Despite this, Golouboff et al. [13] hypothesized that the discrete between-group difference in fear recognition was likely to be due to factors other than laterality of seizures (e.g., differing sample sizes) as groups performed comparably for all other emotions assessed (i.e., anger, disgust, sadness, happiness, neutrality). The two studies that assessed ToM in patients with focal epilepsy have not examined differences as a function of seizure laterality [17,25]. Nevertheless, in two recent studies that we conducted, we found no significant differences between children with left TLE and right TLE on measures of FEP [27] or ToM [26]. The adult literature supports these preliminary results, with two meta-analyses finding no differences between adults with right- and left-sided focal epilepsies in either FEP [28] or ToM [46].

To date, a single longitudinal study has examined FEP following epilepsy surgery in childhood. This study found no change in FEP abilities two years after focal epilepsy resections; FEP impairments were present prior to surgery and persisted postoperatively [18]. This study also found no effect of side of surgery, surgical area (i.e., amygdala resected/in situ), or seizure outcomes on FEP outcomes [18]. These findings parallel results from a review of facial emotion recognition in adults following epilepsy surgery, in which Bora & Meletti [60] found significant FEP impairments both before and after temporal lobe resections, and no differences between pre- and postsurgical groups. In their review, FEP impairments did not differ as a function of the site of surgical resection (i.e., mesial or lateral temporal lobe resection). No published longitudinal or cross-sectional studies have examined ToM in children or adolescents following epilepsy surgery. However, a study of adults with epilepsy found no significant change in ToM following temporal lobe resections, in which surgery included resection of the amygdala for all cases [61].

Finally, prior studies have found no significant relationship between the number of AEDs and FEP [13,18,19] or ToM [16,17,24] in children and adolescents with epilepsy. However, a recent study by Stewart et al. [16] that examined AED dosages found that higher daily dosages of sodium valproate, the most commonly prescribed AED in the sample, correlated with significantly poorer affective ToM in children and adolescents with GGE. This was the first study to examine dosage relationships between AEDs and social cognitive skills in either children or adults with epilepsy. It remains unclear whether these effects were due to reductions in other cognitive skills but is a potentially interesting area for future researchers to explore.

6. Psychosocial correlates of social cognitive impairments in epilepsy

Identifying the psychosocial correlates of social cognitive impairments in children and adolescents with epilepsy is of clinical importance; finding a significant relationship between impaired social cognition and reduced psychosocial functioning in children with epilepsy could provide rationale for including social cognitive screening measures in psychosocial assessments or for developing treatments to target social cognitive difficulties in this patient group. To date, studies have documented significant relationships between impaired ToM and social problems in children and adolescents with epilepsy [16,17,24]. Specifically, impaired performance on an advanced ToM task (i.e., strange stories) has been related to poorer social communication (on the Child Communication Checklist [62]), reduced social competence (on the Child Behavior Checklist [CBCL] [63]), and more peer problems (on the Strength and Difficulties Questionnaire [64]) among children and adolescents with GGE [16,17], TLE [26], and unspecified epilepsy types [24].

Less research has examined the relationship between FEP and social competence. Golouboff et al. [13] found significant correlations between impaired fear recognition and elevated psychosocial problems in children with right TLE, but not left TLE; correlations between impaired fear recognition and psychosocial problems in the group with right TLE were significant for most subscales of the CBCL, including withdrawn, anxious/depressed, social problems, thought problems, attention problems, delinquent behavior, aggression, internalizing, externalizing, and total problems subscales. In contrast, another study found no significant correlation between overall FEP impairment and reduced social competence on the CBCL in children and adolescents with GGE or TLE [27]. Given the modest sample sizes in these two studies (13 to 22 children in each group) and the use of a single rating scale (the CBCL), further investigation is needed to clarify these findings. That social cognition would relate to social functioning in children with epilepsy is supported by two converging theoretical models of social competence proposed for children and adolescents with epilepsy, central nervous system (CNS) conditions [65], neurodevelopmental conditions, and acquired brain disorders [66]. More thorough examination is needed to test these theorized associations in pediatric patients with epilepsy.

7. Discussion

This review has uncovered significant social cognitive impairments in FEP and ToM among children and adolescents with epilepsy, which did not seem to differ depending on whether seizures were generalized or emanating from a specific focal site. The magnitude of overall FEP impairments was comparable in children with generalized and localization-related (i.e., temporal lobe) epilepsies [13,27] and among children with different subtypes of localization-related epilepsy (i.e., TLE and FLE) [13]. Similarly, ToM impairments did not differ between children with generalized and localization-related (i.e., TLE, FLE, extra-TLE/FLE) epilepsies [17,25]. Moreover, three separate studies have found significantly larger impairments in affective ToM relative to cognitive ToM in children with GGE [16], TLE [26], and BECTS [23], suggesting a similar pattern of ToM impairment across subgroups with epilepsy. These results suggest that social cognitive impairments represent a shared feature of epilepsy in childhood.

The overlapping social cognitive profiles that we observed, despite differing etiologies and seizure foci in each group, suggest that a shared underlying neural network of dysfunction may be affected in children with epilepsy, consistent with a neural network account of epilepsy [11,67]. Within this revised approach to classifying epilepsy, seizures are presumed to arise from a diseased network in which overlapping cortical and subcortical structures can be affected regardless of whether seizures emanate from an identified pathological site [11,67]. In contrast, the current findings do not demonstrate a clear-cut mapping of function onto structure, as would be expected from a purely localization account [68]. Within a localization model of epilepsy, one might expect children with seizures emanating from the frontal or temporal lobes to display larger ToM impairments than children without structural lesions/abnormality to these regions (e.g., GGE), given the functional role of the TPJ, mPFC, and frontal and temporal poles in ToM [4,9]. We did not find any evidence to support such a discrepancy between subgroups with epilepsy. Rather, impairments in FEP and ToM were documented across the epilepsies, and the magnitude of impairment was largely comparable between subgroups studied.

Similarly, impairments in social cognition did not relate to other epilepsy factors (i.e., seizure frequency, side of seizure focus, number of AEDs or surgical status) but were related to the age at seizure

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onset and duration of epilepsy. Children with a younger age at seizure onset and longer duration of epilepsy performed more poorly on tasks of FEP [13,19] and ToM [15,24]. These findings suggest that age at seizure onset and duration of epilepsy may be better markers of social cognitive impairment than the site of focal pathology or surgical lesion (if present). It is possible that earlier onset seizures interfere with the initial acquisition of social cognitive skills, and that longer duration of epilepsy stunts the ongoing development of social cognition. For instance, long-term disruption to neurological and social/environmental factors that are important for social cognitive development could impair the ongoing development of these skills throughout childhood. Social and environmental factors are also likely to play a role in the deficits observed, although these have not yet been widely investigated. For example, reduced opportunities for peer interactions or increased need for adult supervision after the onset of epilepsy may impact the development of FEP, ToM, and related social cognitive skills. From a clinical point of view, children with earlier onset and/or more enduring epilepsies may benefit from support to assist with social cognitive deficits; nevertheless, it is likely that all children (including those whose seizures begin in later childhood or adolescence) would benefit from screening to determine whether they require such support, as deficits have been documented independently in child [23] and adolescent [14,16] groups.

7.1. Future research

Knowledge of social cognitive functioning in pediatric patients with epilepsy has expanded over the past decade, however, a number of questions remain unanswered regarding FEP, ToM, other social cognitive skills and the clinical and psychosocial correlates of these difficulties.

First, further research is needed to determine whether emotion-specific FEP impairments are apparent in children and adolescents with epilepsy, or whether inconsistencies documented so far have been due to a combination of small samples and a lack of sensitivity of the measures used. Adopting more fine-grained FEP batteries that present facial emotions at graded valences and have been developed specifically for children, such as the National Institute of Mental Health Child Emotional Faces Set [29] and the Animated Full Facial Expression Comprehension Test [30], may help to clarify results. We recommend using these measures in future studies rather than relying on more widely employed (yet blunter) batteries developed for adults, such as Ekman's pictures of facial affect (POFA) task [22]. In saying this, we believe that acknowledging the presence of FEP impairment (on a whole) may be more important than trying to identify which specific emotions are impaired in different subgroups with epilepsy. Impairments in recognizing facial expressions of emotion are likely to extend beyond the six basic emotions assessed in FEP batteries, and real-world social interactions require children to detect and decode an array of more subtle facial emotion cues. In addition, current neuroimaging evidence does not support the idea that children with different epilepsy subtypes would be impaired in some emotions, but not others. Neuroimaging studies have found that overlapping cortical networks are implicated in processing different facial emotions [32,33]. Moreover, the ability to accurately identify different facial emotions has been found to be strongly correlated in children with [27] and without [51] epilepsy. Thus, it is likely to be more clinically useful and accurate to focus on developing screening tools and treatment methods to assess and address overall FEP impairments in this patient group.

Second, although ToM impairments have been documented in children and adolescents with TLE and FLE, no studies have examined ToM in children with parietal or occipital lobe epilepsies as independent groups. This may be important, as empirical studies and a meta-analysis of adults found that adults with TLE and FLE, but not extra-TLE/FLE, were impaired in ToM compared with healthy controls [46,69]. It is not clear whether these findings are paralleled in children and adolescents with epilepsy. Identifying a possible discrepancy between children with TLE and FLE relative to extra-TLE/FLE would provide important information for detecting and treating ToM impairments, as well as for understanding the neural networks affected in children with seizures emanating from outside the temporal and frontal lobes.

Third, studies have so far focused on FEP and ToM in pediatric patients with epilepsy, yet other sociocognitive skills also play an important role in social and emotional functioning in childhood [2]. The SocioCognitive Integration and Abilities (SOCIAL) model proposed by Beauchamp and Anderson [66] outlines several core sociocognitive skills that contribute to social competence in children, including attribution, empathy, and moral reasoning, in addition to FEP and ToM. Attribution refers to the way individuals attribute intent to behavior (intent attribution) or ascribe lasting personality characteristics to others (trait attribution). Attribution is hypothesized to mediate the relationship between basic face emotion perception and higher-order abilities such as ToM [66]. Moral reasoning, on the other hand, is closely related to ToM and allows individuals to represent perspectives and emotional states to others, understand causal consequences of behavior, and make value judgments about right and wrong [66]. These other aspects of social cognition are equally as important as FEP and ToM for adaptive interpersonal functioning but have not been studied in children, adolescents, or adults with epilepsy [60,70].

Fourth, with respect to the epilepsy-related correlates of social cognition, longitudinal studies are needed to examine the effects of epilepsy surgery on FEP and ToM. To date, only one longitudinal study has examined FEP following focal epilepsy resections [18], and no longitudinal studies have examined ToM following pediatric epilepsy surgery. Studies of adults with epilepsy have found no change in FEP [61] or ToM [60] following epilepsy surgery, but these findings need to be replicated in children and adolescents. The relationship between medication dosages and sociocognitive abilities also requires further examination, as one study found that higher daily dosages of a commonly prescribed AED (i.e., sodium valproate) were significantly correlated with reduced affective ToM [16]. No other studies have examined relationships between AED dosages and social cognition. Further research is needed to better understand relationships between age at seizure onset, duration of epilepsy, and social cognition. It is currently not known whether the onset of seizures marks the start of social cognitive difficulties or whether these impairments predate seizure onset. It is also not known how these skills change across the course of development in children with epilepsy. Social and environmental factors that may affect the development of social cognition (e.g., family environment, peer relationships) are also important to study, as some of these variables may be modifiable and if addressed, could result in better outcomes for children.

Fifth, the relationship between sex, IQ, and social cognition in children with epilepsy requires clarification. In typically developing children, a consistent female advantage has been found for both FEP [34,35] and ToM [40,41]. Only two of the studies included in this review examined sex differences, and neither found significant differences between boys and girls in FEP [18] or ToM [15]. Given the limited literature, it may be important for these differences to be explored further in children with epilepsy. In addition, the relationship between various domains of IQ and social cognition requires further investigation, as findings have been mixed and understanding these relationships may help to detect children who are most at risk of social cognitive difficulties.

Finally, further research is needed to examine the functional implications of social cognitive impairments on children's daily social functioning. Significant relationships have been documented between ToM and social functioning in children and adolescents with epilepsy [16,17,24], and there is preliminary evidence that a specific aspect of FEP (i.e., fear recognition) is related to broader psychosocial difficulties [13]. Given that two converging models of social competence proposed for children with epilepsy, CNS conditions [65], neurodevelopmental

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conditions, and acquired brain disorders [66] purport a relationship between social cognition and social competence, these relationships require further examination among pediatric patients with epilepsy. Specifically, Rantanen, Eriksson, and Nieminen's [65] model hypothesizes that social cognition contributes to three distinct aspects of social competence (i.e., social adjustment, social performance, and social skills) in children with epilepsy and CNS conditions. Beauchamp and Anderson's [66] SOCIAL model hypothesizes a relationship between various aspects of social cognition (i.e., FEP, attribution, ToM, empathy, and moral reasoning) and social competence. Thus, the relationship between basic and higher-order social cognitive skills with broad aspects of social competence needs to be investigated.

7.2. Clinical implications

There are several important clinical implications from these findings, which may affect screening and treatment procedures for pediatric patients with epilepsy. First, routine neuropsychological testing of children and adolescents with epilepsy should include measures of social cognition. At present, assessments are still heavily focused on general cognitive skills [71]. These assessments do not consider important socioemotional aspects of epilepsy, which appear to be a defining feature of epilepsy in childhood. Although validated social cognitive screening tools have not been developed for pediatric patients with epilepsy, measures developed for broader child and adolescent populations may be of use. The Pediatric Evaluation of Emotions, Relationships, and Socialization is a newly developed measure that provides a computerized platform for assessing socioemotional, social cognitive, and social functioning in children [72]. In addition, the NEPSY-II includes a Social Perception domain with two general subtests assessing FEP and ToM [73]. The validity of these measures still requires evaluation among children with epilepsy, and it remains unclear whether specialized screening tools need to be developed for this group. Moreover, caution should be taken in interpreting results from the NEPSY-II subtests as they are relatively brief and may not be as sensitive as more comprehensive measures; nevertheless, they are a good starting point given that more comprehensive and validated measures are not yet widely available.

Another interesting clinical implication relates to detection and diagnosis of autistic features or ASD in children with epilepsy. Epilepsy and ASD are highly comorbid, with the prevalence of children with epilepsy who also meet criteria for ASD estimated to be 20% [74] to 32% [75]. The literature on where epilepsy and ASD overlap is still emerging, in terms of both neurobiological underpinnings and observable social, cognitive, and behavioral features [76]. Nevertheless, social cognitive impairments appear to be a shared feature of both epilepsy and ASD and may represent a diagnostic border of these two neurodevelopmental conditions in childhood [77]. The presence of social cognitive deficits in both epilepsy and ASD also provides insight into the brain networks affected in these conditions, as well as those implicated in social cognitive processes more broadly. Epilepsy and ASD are both regarded as neural network disorders that affect connectivity of dispersed cortical and subcortical structures [11,78], and it has been hypothesized that the neural mechanisms that lead to epilepsy and ASD also affect the development of social cognition [74]. Whether deficits in FEP and ToM are comparable in children diagnosed with either epilepsy or ASD or indeed children with comorbid diagnoses of both conditions, require further examination, as prior studies of children with epilepsy have excluded children with ASD [77]. Understanding how social cognitive deficits manifest in children will assist with developing more appropriate therapeutic interventions for children with epilepsy in accordance with an ASD phenotype.

From a treatment perspective, interventions targeting social cognition (especially ToM, which has been related to social competence problems in children with epilepsy [16,24]) may be an effective way of addressing social difficulties in this group. Theory of Mind interventions have been found to improve ToM and broader social functioning among children with other neurodevelopmental conditions, such as ASD, hearing impairment, and typically developing children with social handicaps [79,80]. A recently published study protocol outlined a novel cognitive behavioral intervention with ToM training developed specifically for children with epilepsy [81]. This is the first program that we are aware of to address social impairments in children with epilepsy. Evaluation of this and other programs designed to address social difficulties in young patients with epilepsy should be prioritized in future research, as validated psychosocial interventions to address social difficulties for this group do not currently exist [82].

8. Conclusions

This review has shown that social cognitive abilities, including FEP and ToM, are impaired in children and adolescents with epilepsy. At present, there is little evidence for clear differences in the social cognitive abilities of children with different epilepsy subtypes; rather, social cognitive impairments appear to represent a shared feature of epilepsy in childhood. The current results support the revised phenomenological approach to classifying epilepsies and seizures outlined by the ILAE [11], which proposes that a shared neural network underlies seizures, as well as the cognitive and behavioral phenotypes that manifest in this condition. Further research is needed to examine the functional implications of social cognitive impairments on children's daily social functioning, as well as to evaluate screening tools and treatment methods to identify and address these difficulties.

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None.

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