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Research Article

Social Cognition in Idiopathic Generalized Epilepsies and Nonlesional Temporal Lobe Epilepsy

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Objectives. Social cognition (SC) is a multifaceted concept involving mental processes to understand, store, and apply information regarding social relationships. Brain lesions in key areas can impair critical components of SC, but seizures and epileptiform discharges could also be associated with deficits in SC. To verify this hypothesis, this study evaluated SC in persons with generalized or focal epilepsy without detectable brain lesion. *Materials and Methods*. Forty-eight adult persons with idiopathic generalized epilepsy (IGE) or temporal lobe epilepsy without brain lesion (cryptoTLE) and 24 healthy controls were evaluated by means of the Faux Pas Test (FPT), Social Situation Test (SST), Moral/Conventional Distinction Test (MCDT), and Empathy Questionnaire (EQ) which assess theory of mind (ToM), recognition of social behaviors and moral and conventional rules, and empathy. Clinical work-up included information on age at seizure onset, epilepsy duration, seizure symptoms and frequency, demographic characteristics, and the presence of comorbidities. *Results*. Compared to controls, persons with IGE or cryptoTLE were impaired in the understanding of existent faux pas on the FPT. On the SST, persons with cryptoTLE also showed significant deficits, whereas the IGE persons only were less accurate in recognizing normative behaviors. In cryptoTLE persons, the capacity to recognize cognitive and affective mental states correlated with seizure frequency and age, whereas, in IGE persons, the SST and MCDT scores correlated with schooling and age, respectively. *Conclusions*. CryptoTLE can cause extensive deficits in ToM and recognition of social situations, whereas IGE is only associated with deficits in fewer domains. Dysfunction of temporolimbic areas could be related to seizure frequency and associated with more severe SC impairment in cryptoTLE. Older age and poor education may be associated with SC deficits in focal or generalized epilepsy.

1. Introduction

Social cognition (SC) is a higher-order cognitive domain including the recognition and elaboration of interpersonal relationships and their use to guide social behavior [1, 2]. It is a complex domain that encompasses comprehension of others' mental states, empathy, emotion processing, appreciation of interpersonal relationships, and moral judgment and supports the understanding and guidance of others' and one's own behavior, impacting on the success of human relationships, quality of life (QoL), and autonomy [3]. Theory of mind (ToM) is a key component of SC, described as the capacity to attribute mental states such as beliefs, intentions, desires, lies, and affective status to others and oneself and to predict one's own and others' behavior based accordingly [4]. Neuroimaging studies documented involvement of a widespread neural network encompassing the medial and orbital prefrontal cortices, inferolateral temporal cortex, superior temporal sulcus, amygdala, and temporoparietal junction [5, 6]. The ventromedial prefrontal, inferior-lateral temporal and parietal cortex, and temporo-parietal junction also support empathy, while the prefrontal cortex is also related to moral judgment [7].

Over the past decade, a growing number of studies have shown that the SC is impaired in persons with epilepsy [1]. What is not clear, however, is whether such cognitive impairments are generally related to structural brain lesions or to the effect of seizures in key areas of SC.

Most information about this issue has been obtained from investigations of other cognitive functions, suggesting that persons with temporal lobe epilepsy (TLE) may have subtle cognitive deficits even in the absence of any structural abnormalities and that at least part of the cognitive impairment may be the result of the effect of the seizures and subclinical epileptiform discharges [8–11]. In contrast, studies of SC in epilepsy have been focused mainly on focal epilepsies associated with brain lesion, yet provided little and conflicting information about idiopathic generalized epilepsies (IGE) and cryptogenetic epilepsies (CE) [10].

Compared to healthy controls (HC), persons with temporal lobe epilepsy (TLE) reported deficits in facial emotion recognition, especially with the emotions of fear and sadness [12], recognition and comprehension of others' mental states, and understanding of sarcastic speech in social exchanges [13]. Indeed, Giovagnoli et al. [7] described impairment in advanced ToM components and in distinguishing normative behaviors and violations but preservation of empathy and sensitivity to moral and conventional rules in a group with TLE. Furthermore, additional explorations have revealed a relationship between ToM impairment and early age of seizure onset, disease duration, and the number of antiseizure medication (ASM) [14, 15]. Similarly, impairment in recognition of negative emotions, ToM, and empathy has been widely described in persons with frontal lobe epilepsy (FLE) [16]. In comparison with persons with TLE, persons with FLE show both more severe and more extensive ToM impairments characterized by altered recognition and comprehension of existent mental states, but adequate capacity to exclude nonexistent mental states. For this reason, it has been suggested to consider ToM deficits to be a marker of FLE neurobehavioral phenotype, being able to discriminate these patients from other patients and healthy subjects [15–17].

In contrast, little attention has been given to SC in patient with idiopathic generalized epilepsies (IGE) and persons with cryptogenetic epilepsy, with conflicting findings [18]. Although, in these patients, seizures do not emanate from either the frontal or temporal lobes, generalized discharges could interfere with SC networks [18]. Moreover, persons with IGE exhibit subtle brain structural alterations in mesial prefrontal and temporoparietal cortices [1]. In recent years, most studies of SC in persons with IGE have focused on emotion recognition reporting impairment in recognition of disgust, fear, and anger [18–20]. In contrast, only a few studies have investigated other aspects of SC such as social judgment and empathy, documenting impaired perspective-taking and cognitive empathy abilities [21] but an average capacity to judge the appropriateness of behavior in specific social contexts [22]. A meta-analysis found that persons with IGE are also at risk of ToM deficit [23]. The most consistent impairments have been documented on advanced ToM story tasks, such as the strange stories and Faux Pas Tests (FPT) [24, 25]. However, Realmuto et al. [18] found a mental state attribution deficit in persons with TLE but not in those with IGE. Similarly, Morou et al. [13] found significant ToM impairment in persons with focal epilepsy in comparison with healthy subjects and IGE persons on comprehension of hinting, sarcasm, metaphor, false beliefs, and deception, with the exception of faux pas on which the group with IGE also performed more poorly than the healthy group.

In brief, focal and generalized epilepsies can cause different SC deficits, with no definite or mild impairment in IGE and significant impairment in focal epilepsies starting from the temporal or frontal lobe. Structural brain lesions associated with TLE or FLE can impair in particular, ToM, and the understanding of behavior appropriateness in social contexts. In addition, it may be expected that seizures and epileptiform discharges would also affect the SC neural system. We performed this study to try mainly to clarify the type and severity of impairment of SC in generalized and focal epilepsies in the absence of detectable brain lesions and to explore the relationship between seizures and SC impairments. To do this, we investigated persons with IGE or TLE without neuroimaging-detected brain lesion (cryptoTLE) by using a battery of tests to assess aspects of social cognition.

2. Material and Methods

2.1. Participants. This was a cross-sectional observational study. We evaluated a series of adult persons with IGE or cryptoTLE who had been referred to four Italian epilepsy centers. Forty-eight persons (32 women) with cryptoTLE ($n = 24$, 12 right cryptoTLE, and 12 left cryptoTLE) or IGE (7 juvenile myoclonic epilepsy, 17 generalized tonic–clonic seizures alone) and 24 healthy controls were consecutively selected and evaluated.

Persons with cryptoTLE did not show mesial temporal sclerosis or other structural brain lesions on magnetic resonance imaging (MRI), and the nature of the underlying cause is not currently known. All patients received detailed medical and neurological examinations carried out by a neurologist with special expertise in epilepsy. The diagnosis was made according to ILAE criteria [26], based on seizure symptoms, electroencephalographic (EEG) features, and MRI results. Data was collected during the neurological visits and included information on age at seizure onset, epilepsy duration, seizure symptoms and seizure frequency, demographic characteristics, and the presence of comorbidities. Seizure frequency was measured as the mean number of seizures a month during the six months preceding neuropsychological assessment, while background socio-demographic data were obtained as described in the World Health Organization Quality of Life 100 inventory [27]. High-income level has been classified according to criteria reported by Lee et al. [28] which considered the total household income (TSI) in previous year (low-income level, TSI

< 19,999€; middle-income level, TSI 19,999-49,999€; TSI > 50,000€).

Eligibility criteria included chronological age ≥ 18 years, years of schooling ≥ 5, average abstract reasoning (Raven's Colored Progressive Matrices (RCPM) score greater than 17.5) [29], verbal comprehension (Token Test (TT) score greater than 26.25) [30], and no symptoms of autism spectrum disorders at clinical history. Although specific instruments are important to exclude strict diagnosis of autism, the presence of autism spectrum disorders was excluded on the basis of clinical history and clinical examination. Persons with a history of psychiatric illness (major depression, psychosis) and serious medical illnesses (cancer, heart, liver or kidney failure, metabolic diseases, respiratory illnesses, systemic neoplasms, insulin-dependent diabetes, and immune-mediated disorders) were excluded. Moreover, their clinical history was negative for intellectual disability. Based on these criteria, 6 people with TLE epilepsy and 2 with IGE were excluded.

The controls were recruited among the hospital staff and visitors if they had negative neurological and psychiatric history and were matched to the patients in chronological age (±5), years of schooling (±3), and sex distribution.

The study protocol was approved by the hospital review board, and all of the participants gave their written informed consent before any study-related procedure was performed, in accordance with the Declaration of Helsinki.

2.2. Assessment of Social Cognition. Patients and controls were administered a neuropsychological battery assessing main components of SC, including the Faux Pas Tests (FPT) [31], Social Situation Test (SST), Moral/Conventional Distinction Test (MCDT) [32], and Empathy Questionnaire (EQ) [33].

The FPT has been described in detail in Stone et al. [31]. It requires a subject to acknowledge or rule out the presence of a social faux pas (FP) in 20 stories (10 with and 10 without FP). After reading each story, subjects are asked if someone said something that would hurt or upset another person. If they answer yes, they are asked four questions that investigate identification of character making FP, appreciation of behavior appropriateness, intentions recognition, and comprehension of affective mental states. A control question is asked at the end of each story to verify if the subject has understood the contextual details. The FPT provided nine scores: two detection scores indicating the recognition of an FP and the rejection of a non-FP, two control scores, four comprehension scores (each ranging from 0 to 10), and one total comprehension score that is the sum of the 4 comprehension questions with a score between 0 and 40. According to previous reports [34], the mean FPT comprehension score (ToM measure) was estimated to be 30.65 (SD 8.69) in early onset pharmacoresistant epilepsy TLE persons, 33.65 (SD 7.49) in late onset pharmacoresistant TLE persons, and 38.30 (SD 2.74) in healthy subjects.

The MCDT is a part of a social intelligence battery by Prior et al. [32]. The test investigates the knowledge of moral rules based on one's own conscience and relating to a choice between good and bad that is not necessarily collectively shared and conventional rules that are not universal but relate to local customs, context, and authority. It includes six scenarios containing moral transgressions and six scenarios containing conventional transgressions from Blair [35]. Four questions were asked to determine whether the subjects consider the transgressive action to be wrong and, if so, how serious it is and whether the subjects think that the wrongness of the transgression is "authority dependent."

Participants scored either 0 or 1 according to whether they answered the permissibility question "Was it right for X to do Y?" as right or wrong, respectively. Thus, if all six moral and six conventional transgressions were correctly considered impermissible, the participant would score the maximum of 6 for both the moral and conventional transgressions (permissibility score).

For transgressions correctly identified as nonpermissible, the participants were asked to rate the seriousness of the transgression on a scale of 1–10. The maximum seriousness score for both types of transgression was thus 60. The number of transgressions judged as nonpermissible in the absence of rules (absent rules score) was calculated from answers to the final two questions (range 0-12). Interrater reliability was high (91%) [35].

The SST is a part of a social intelligence battery by Prior et al. [32] and investigates the ability to judge the adequacy of people's behavior in the social environment and distinguishes normative behavior from violation of common social norms that generally generate disapproval. The subjects read text passages pertaining to 25 situations encompassing ordinary and unusual behavior and were asked to rate the social appropriateness of each behavior using an A-D scale, where A was attributed to fairly normal, B to rather strange, C to very eccentric, and D to shocking behavior. Three scores were calculated: one for the correct identification of ordinary behaviors (range 0–15), one for the correct identification of violations (range 0–25), and one describing the weight assigned to each violation (range 0–75).

The EQ includes 40 statements with which the subject is asked to decide whether he/she fully agrees, quite agrees, quite disagrees, or completely disagrees. Participants received 0 for a "nonempathic" response, whatever the magnitude, and 1 or 2 for an "empathic response" depending on the strength of the reply. The total score is out of 80, and cut-off is equal to or fewer than 30 points [33]. The authors suggest that as the split-half reliability is high (0.84), the items are likely to tap a single construct. Test-retest reliability for the EQ was $r = 0.97$, which is also highly significant ($p < 0.001$), and moderate associations were found between the EQ and IRI subscales, suggesting concurrent validity.

2.3. Assessment of Other Cognitive Functions. In order to contextualize SC, standardized neuropsychological tests were used to evaluate attention (attentive matrices (AM)—it consists of a series of patterns of numbers; the patient is required to check the numbers to find a target number (from one to three digits)) [36], visuomotor coordination speed (trail making test A (TMTA)—the test requires the patient to connect 25 randomly placed circles in ascending numerical order), set shifting (trail making test B (TMTB)—the test requires to connect numbers and letters in an alternating progressive sequence, 1 to A, A to 2, 2 to B, and so on) [37], lexical-semantic retrieval on semantic cues (word fluency- (WF-) semantic) and on phonemic cues (WF-phonemic) (the semantic fluency is tested by asking the examinee to generate semantic category exemplars, names of animals, names of fruits, and automakers, and phonemic fluency, assessed by asking the examinee to generate words beginning with the letters F, P, and L) [38], immediate memory (digit span (DS)—for the task, the individual repeats numbers spoken by the examiner), working memory (Corsi block span (CBS)—in this test, there are cubes that are tapped by the examiner in novel sequences of increasing length after which participants are required to reproduce each sequence immediately) [39], long-term verbal (short story (SS)—the examiner reads a short story and asks the patient to repeat it immediately. The story is reread and asked to repeat it after 10 minutes) [40], and visuospatial (Rey complex figure- (RCF-) recall) memory and constructive praxis (RCF-copying) (the patients are asked to reproduce a complicated line drawing, first by copying it freehand, and then drawing from memory (recall after 15 minutes)) [41].

2.4. Data Analysis. Nonparametric Kruskal-Wallis one-way analysis of variance (ANOVA) was used to compare chronological age and years of schooling between controls and patients as a single group. Chi-square tests were used to compare gender distribution, marital status, type of occupation, income level, and residence (rural, urban). The Mann–Whitney test was used to compare clinical variables (age at epilepsy onset, disease duration, monthly seizure frequency in previous six months, and ASM number) between IGE and cryptoTLE.

Separate Kruskal-Wallis one-way ANOVAs were used to compare the score sets provided by the FPT, MCDT, SST, and EQ separately, setting the significance level as $p \leq 0.003$ based on Bonferroni's rule for 16 comparisons.

The Spearman rank correlation coefficient evaluated the correlation between the SC test scores and seizure frequency, chronological age, and years of schooling. Significance level was set as $p < 0.02$ based on Bonferroni's rule for 3 correlations. Logistic regression analysis was applied to explore factors predicting membership of the patient and control groups.

In order to classify the patients' individual performance, the FPT, RBSS, SMCR, and EQ z scores were compared with the percentiles derived from the controls' z scores (8th percentile or below, 9th–24th percentile, 25th–74th percentile, and 75th percentile or above) [42]. The memory, attention, coordination, set shifting, verbal initiative and fluency, and constructive praxis age- and schooling-adjusted scores were compared with the cut-off values provided by published normative studies, classifying the individual performance into average and impaired [36–41].

3. Results

3.1. Patients. The persons with cryptoTLE or IGE and the controls were very similar in terms of chronological age ($p = 0.61$) and years of schooling ($p = 0.128$), sex distribution ($p = 1$), marital status ($p = 0.51$), type of occupation ($p = 0.91$), and income level ($p = 0.2$). The groups did not differ in age ($p = 0.06$) at the time of seizure onset, epilepsy duration ($p = 0.26$), monthly seizure frequency during the last year ($p = 0.06$), and ASM number ($p = 0.35$) (Table 1).

Based on normative data [36–41], 93.8% and 81.3% of the patients showed average performance on the AM and CBS, respectively, putting in evidence adequate attention and working memory. On the TMTA and TMTB, 18.7% and 14.6% of patients were, respectively, impaired. On the contrary, from 8.5% to 37.5% of patients were impaired on the DS, SS, RCF-recall and RCF-coping, WF-phonemic, and WF-semantic, indicating more frequent memory, lexical-semantic retrieval, and constructive praxis deficits. The IGE and cryptoTLE persons showed very similar frequencies of equivalent score (Table 2).

3.2. Social Cognition. All patients and controls completed the SC tests. Table 3 summarizes the mean test scores; Table 4 describes statistical outputs of the Mann–Whitney tests and effect sizes provided by the Mann–Whitney tests. Compared to controls, persons with cryptoTLE or IGE obtained the same scores on the no-FP exclusion question, demonstrating adequate capacity to distinguish existent and non-existent FPs. On the contrary, the patients showed significant impairments in the understanding of real faux pas on the FPT and in comprehending others' intentions and cognitive and affective mental states. In particular, the Kruskal-Wallis one-way ANOVA comparing the patient and control groups revealed a significant influence for group on the first, second, third, and fourth comprehension question and total comprehension question ($p < 0.001$). Post hoc Mann–Whitney tests showed that, in comparison with controls, persons with cryptoTLE had significantly lower scores on the first ($p = 0.001$), second ($p < 0.001$), third ($p < 0.001$), and fourth ($p < 0.001$) question and total comprehension ($p < 0.001$), while persons with IGE had lower scores on the first ($p = 0.001$), second ($p < 0.001$), third ($p < 0.001$), and fourth ($p < 0.001$) question and total comprehension ($p < 0.001$). The patient groups did not differ between them. Patient percentages with impaired and optimal FPT performance were significantly greater and smaller, respectively, in comparison with control percentages ($\chi^2(3) = 35.32$, $p < 0.001$).

The Kruskal-Wallis one-way ANOVA also showed a significant influence for group on the SST, with significant in recognition of normative behaviors ($p = 0.003$) and minor differences in recognition of violations ($p = 0.03$) and appreciation of severity of violations ($p = 0.033$). In comparison with the controls, the persons with cryptoTLE showed significant deficits in recognizing normative behaviors ($p < 0.001$) and only slight tendency for recognition of violations ($p = 0.014$) and appreciating severity of behavior violations ($p = 0.018$), whereas the persons with IGE were only mildly impaired in the recognition of normative behaviors ($p = 0.017$). The patient with IGE performed better than the persons with cryptoTLE on recognition of violations ($p = 0.046$) and on appreciation of the severity of behavior violations ($p = 0.042$),

Table 1: Sociodemographic and clinical aspects of persons with idiopathic generalized epilepsies, cryptogenic temporal lobe epilepsy, and healthy controls.

	HC ($n = 24$)	Patient subgroups IGE ($n = 24$)	Patient subgroups C-TLE($n = 24$)
Epilepsy-related factors			
Chronological age	40.08 ± 15.14	38.13 ± 16.77	35.75 ± 13.13
Years of schooling	12.67 ± 3.09	11.29 ± 3.43	13.08 ± 2.92
Males/females	8 : 16	8 : 16	8 : 16
Marital status			
Unmarried	11	14	13
Married	9	10	9
Separated/divorced	3	0	2
Widowed	1	0	0
Occupation			
Student	4	6	6
Unemployed	2	2	3
Homemaker	2	3	2
Employed	14	12	13
Retired	2	1	0
Income level			
Low	7	8	3
Average	16	16	18
High	1	0	3
Age at time of epilepsy onset		20.58 ± 15.71	21.12 ± 12.71
Epilepsy duration (years)		17.45 ± 15.41	14.20 ± 13.34
Seizure frequency		0.69 ± 0.83	0.94 ± 1.25
Number of ASM		1.42 + 0.58	1.75 + 1.03

Abbreviations: IGE = idiopathic generalized epilepsies; C-TLE = cryptogenic temporal lobe epilepsy; ASM = antiseizure medication; HC = healthy controls.

albeit the difference was not significant. Compared to controls, the percentages of patients with impaired and optimal SST performance were significantly greater and smaller for normative behaviors (χ^2 (3) = 17.80, $p = 0.007$) and were very similar for violations (χ^2 (3) = 8.57, $p = 0.19$).

The controls and persons with IGE or cryptoTLE had similar EQ and MCDT scores. The percentages of patients and controls with scarce, borderline, average, or optimal performance were very similar on recognition of the severity of the disregard of moral rules (χ^2 (3) = 1.03, $p = 0.60$), conventional rules (χ^2 (3) = 0.62, $p = 0.73$). Finally, the percentages of patients and controls with scarce, borderline, average, or optimal EQ performance were very similar (χ^2 (3) = 3.92, $p = 0.69$).

3.3. Correlation Analysis. The Spearman coefficient showed that, in cryptoTLE persons, the second comprehension score significantly correlated with seizure frequency ($p = 0.020$), and the first ($p = 0.028$) and fourth comprehension scores ($p = 0.028$) had an almost significant correlation. In addition, the FP recognition ($p = 0.003$) and the first ($p = 0.001$) and second comprehension scores ($p = 0.018$) significantly correlated with chronological age. In IGE persons, the MCDT recognition of severity of moral rule transgression score ($p = 0.018$) significantly correlated with age, while the SST recognition of normative behavior score significantly correlated with years of schooling ($p = 0.014$) (Table 5).

Separate binary logistic regression analyses explored the ability of FPT comprehension and SST recognition scores of normative behaviors, chronological age, and years of schooling, which were significant in the Kruskal-Wallis and Spearman analyses, in predicting patient or control group membership. The analysis of cryptoTLE and HC provided a consistent pattern ($\chi^2(1) = 28.97$, $p < 0.001$): the FPT total comprehension score had a significant effect ($B = -0.42$, $\text{Exp}(B) = 0.66$, $p = 0.001$) allowing correct classification of 66.7% of patients and 87.5% of controls. The analysis of IGE and HC also provided a consistent pattern ($\chi^2(1) = 31.16$, $p < 0.001$): the third comprehension FPT score had a significant effect ($B = -0.97$, $\text{Exp}(B) = 0.38$, $p < 0.001$) allowing the correct classification of 87.5% of patients and 79.2% of controls. No variables had a predictive value in the analysis of cryptoTLE and IGE.

4. Discussion

It is known that focal epilepsies can impair SC, while minor deficits may be encountered in generalized epilepsies [13–18]. This study was thought to clarify the type and

Table 2: Neuropsychological test scores in persons with idiopathic generalized epilepsies and cryptogenic temporal lobe epilepsies.

Neuropsychological tests	Cut-off[a]	Adjusted scores[b]	Equivalent scores[c]								
			0			1			2-4		
			IGE	C-TLE	All patients	IGE	C-TLE	All patients	IGE	C-TLE	All patients
Attentive matrices	<31	53.56 ± 7.36	12.5%	0%	6.2%	0%	0%	0%	87.5%	100%	93.8%
Trail making test A	>93	61.98 ± 33.62	16.7%	20.8%	18.7%	12.5%	20.8%	16.7%	70.8%	58.4%	64.6%
Trail making test B	>282	160.46 ± 102.14	8.3%	20.8%	14.6%	16.7%	16.7%	16.7%	75%	62.5%	68.7%
Digit span	<3.75	5.06 ± 1.39	20.8%	41.7%	31.2%	12.5%	8.3%	10.4%	66.7%	50%	58.4%
Corsi block span	<3.5	4.35 ± 0.86	12.5%	8.3%	10.4%	12.5%	4.2%	8.3%	75%	87.5%	81.3%
Word fluency on phonemic cues	17	24.79 ± 12.44	25%	50%	37.5%	12.5%	16.7%	14.6%	62.5%	33.3%	47.9%
Word fluency on semantic cues	25	32.54 ± 10.35	20.8%	29.2%	25%	25%	25%	25%	54.2%	45.8%	50%
Rey complex figure copying	28.88	32.30 ± 3.59	8.7%	25%	16.8%	0%	29.2%	14.6%	91.3%	45.8%	68.6%
Rey complex figure delayed reproduction	9.47	13.17 ± 5.53	8.7%	8.3%	8.5%	30.4%	29.2%	29.8%	60.9%	62.5%	61.7%

Abbreviations: IGE = idiopathic generalized epilepsies; C-TLE = cryptogenic temporal lobe epilepsy. The percentages refer to the proportions of patients in each category. [a]Cut-off values based on published normative studies. [b]Age- and schooling-adjusted scores. [c]The equivalent scores correspond to five categories of performance in healthy subjects: 0 = deficit, 1 = borderline, and 2 to 4 = good to optimal performance.

Table 3: Social cognition test scores in persons with idiopathic generalized epilepsies, cryptogenic temporal lobe epilepsy, and healthy controls.

	HC[a]	Patients subgroups IGE[a]	Patients subgroups C-TLE[a]	All participants[a]
Faux Pas Test				
Exclusion of nonfaux pas	9.62 ± 1.10	9.45 ± 1.82	9.54 ± 1.35	9.54 ± 1.43
Recognition on faux pas	9.46 ± 0.72	8.12 ± 1.92	7.87 ± 2.38	8.18 ± 2.00
First question	9.5 ± 0.59	7.58 ± 2.10	7.37 ± 2.63	7.84 ± 2.20
Second question	9.12 ± 1.07	6.67 ± 1.93	6.46 ± 2.60	7.17 ± 2.28
Third question	8.67 ± 1.43	6.02 ± 2.10	4.75 ± 2.54	6.20 ± 2.51
Third question	9.00 ± 1.02	6.75 ± 1.96	6.29 ± 2.44	7.06 ± 2.22
Total comprehension	36.29 ± 3.57	27.16 ± 6.88	24.79 ± 8.77	29.41 ± 8.32
Social Situation Test				
Normative behaviors	14.08 ± 1.14	13.08 ± 1.77	11.96 ± 3.73	13.06 ± 2.57
Violations	23.20 ± 2.67	23.00 ± 2.32	21.29 ± 3.34	22.57 ± 2.92
Severity of violations	52.33 ± 10.36	50.96 ± 9.71	45.37 ± 10.53	49.90 ± 10.84
Moral/Conventional Distinction Test				
Recognition of moral rules	6 ± 0	5.95 ± 0.20	5.96 ± 0.20	5.97 ± 0.17
Recognition of the severity of disregard of moral rules	52.50 ± 6.76	50.96 ± 10.64	53.83 ± 6.49	52.26 ± 8.19
Recognition of moral rules in the absence of expressed norms	11.29 ± 1.65	11.17 ± 1.93	11.58 ± 1.28	11.24 ± 1.71
Recognition of conventional rules	5.79 ± 0.41	5.66 ± 0.56	5.75 ± 0.53	5.70 ± 0.52
Recognition of the severity of disregard of conventional rules	40.37 ± 10.34	34.42 ± 15.17	41.21 ± 12.28	39.10 ± 12.94
Recognition of conventional rules in the absence of expressed norms	9.91 ± 2.68	9.00 ± 3.59	10.10 ± 2.72	9.49 ± 3.14
Empathy Questionnaire	46.04 ± 12.77	47.04 ± 10.45	47.37 ± 8.94	46.82 ± 10.70

Abbreviations: IGE = idiopathic generalized epilepsies; C-TLE = cryptogenic temporal lobe epilepsy; HC = healthy controls. [a]Raw scores.

severity of impairment of SC in generalized and focal epilepsies in the absence of detectable brain lesions, also exploring the relationship between epilepsy-related factors and SC deficits.

Results confirmed impairments primarily among persons with focal epilepsy and more circumscribed difficulties among persons with generalized epilepsy. Specifically, cryptoTLE demonstrated difficulty with attribution in understanding who committed an FP, judging the appropriateness of offensive sentences ("why wouldn't she/he have said that?"), and distinguishing intentional behaviors. Consistent with previous studies [7], these results revealed that persons with cryptoTLE were also significantly impaired in SST, suggesting that cryptoTLE can affect the capacity to distinguish normative behaviors, to recognize violations, and to appreciate their severity. Furthermore, the FPT total comprehension score significantly predicted cryptoTLE membership compared to the control group, highlighting the importance of ToM deficits for the diagnosis of the cognitive phenotype in this condition.

Although these patients showed no structural brain lesions at MRI, it is worth noting that we cannot exclude primary structural differences between the brains of the subjects and normal controls. The deficits of SC may be caused by malfunctioning of medial and lateral temporal lobe structures and fronto-limbic areas implied in SC. This alteration could be primary, before the onset of the seizures or any epileptiform discharges, or secondary, as result of the pathophysiological effects of seizures and subclinical epileptiform discharges. The significant correlation observed between seizure frequency and the ability to recognize others' beliefs in the cryptoTLE, but not in the IGE, may support the hypothesis that repeated seizures might be associated with increased damage of the SC network underlying the SC. In this regard, previous studies also suggested that epileptic discharges, rather than MRI-detected brain lesions, may be related to cognitive deficits in learning and memory in persons with TLE [8–11]. Similarly, Deutsch [43] found that persons with epilepsy with or without overt brain damage were similarly impaired on learning and memory tests.

Regarding the group with IGE, the present study showed similar deficits to the cryptoTLE group on the FPT, and the FPT third comprehension score also predicted IGE membership compared to the control group. Altered SC could be explained, at least in part, by the involvement of frontal/fronto-temporal dysfunction also in the physiopathology of IGE, in line with previous imaging and neuropsychological studies [1, 44]. According to some studies on children and adolescents, these difficulties could be linked to some characteristics of epilepsy itself; for instance, deficits in the recognition of facial emotions are potentially related to difficulties in nonverbal intelligence or executive functions. This could also be a starting point for future studies on adults [45].

Table 4: Statistical value of the Mann–Whitney test scores attained in social cognition evaluation tests.

	IGE vs. HC			C-TLE vs. HC			C-TLE vs. IGE		
	p value[a]	U	Effect size	p value	U	Effect size	p value	U	Effect size
Faux Pas Test									
Exclusion of nonfaux pas	0.133	226	0.05	0.892	283	0.000	0.315	244.000	0.021
Recognition on faux pas	0.002*	150.5	0.19	0.010*	169.500	0.142	0.933	284.000	0.000
First question	<0.001*	114.500	0.29	<0.001*	115.500	0.293	0.983	287.000	0.000
Second question	<0.001*	74.000	0.43	<0.001*	102.500	0.326	0.975	286.500	0.000
Third question	<0.001*	93.000	0.35	<0.001*	52.00	0.519	0.068	200.500	0.071
Fourth question	<0.001*	70.500	0.44	<0.001*	66.00	0.465	0.816	277.00	0.001
Total comprehension	<0.001*	54.500	0.49	<0.001*	47.500	0.526	0.358	243.500	0.017
Social Situation test									
Normative behaviors	0.017	176.500	0.120	0.001*	130.00	0.238	0.031	240.500	0.021
Violations	0.52	258.500	0.008	0.014	171.00	0.127	0.046	192.500	0.084
Severity of violations	0.51	256.00	0.009	0.018	173.00	0.119	0.042	189.500	0.088
Moral/Conventional Distinction Test									
Recognition of moral rules	0.317	276.00	0.021	0.317	276.00	0.021	1.000	288.00	0
Recognition of the severity of disregard of moral rules	0.843	278.500	0.000	0.436	250.500	0.012	0.706	270.00	0.003
Recognition of moral rules in the absence of expressed norms	0.942	285.500	0.000	0.650	273.00	0.004	0.596	270.500	0.005
Recognition of conventional rules	0.468	261.500	0.011	0.942	285.500	0.000	0.530	265.00	0.008
Recognition of the severity of disregard of conventional rules	0.445	251.00	0.012	0.687	268.500	0.003	0.392	246.500	0.015
Recognition of conventional rules in the absence of expressed norms	0.604	264.00	0.005	0.687	269.500	0.003	0.393	249.00	0.015
Empathy Questionnaire	0.457	252.00	0.011	0.375	245.000	0.016	0.844	278.500	0.001

Abbreviations: Symbol "*" marks significant correlations ($p \leq 0.02$). IGE = idiopathic generalized epilepsies; C-TLE = cryptogenic temporal lobe epilepsy; HC = healthy controls. [a]$p < 0.003$.

On the SST, IGE persons did more poorly than the controls only on recognition of normative behaviors but performed similarly on recognition of violations and appreciation of the severity of behavior violations. However, when compared with the cryptoTLE group, persons with IGE performed higher on recognition of violations and appreciation of the severity of behavior violations. Although these differences do not reach the statistical significance, we think that these tendencies highlight more extensive impairment in SC abilities in persons with cryptoTLE compared with persons with IGE. A possible reason for this difference is that seizures and epileptiform discharges starting from the temporal lobe might provoke a greater and more extensive dysfunction in SC circuitry including the temporoparietal junction, temporal pole, and medial prefrontal cortex than generalized seizures.

Preservation of empathy and moral/conventional rule recognition in persons with cryptoTLE or IGE suggests minor vulnerability of these SC components to generalized pathophysiological abnormalities. Resistance of empathy and recognition of moral/conventional rule to seizures may also reflect a strong relation of these functions to psychological and personality traits and consolidated social habits [7].

Moreover, in IGE persons, formal education, as expressed by the years of schooling, was correlated with the capacity to recognize normative behaviors which are considered appropriate by healthy people on the basis of acquired social norms in a given context. We suggest that persons with epilepsy, despite having the same educational level as controls, may have a lower quality educational experience than controls due to seizure-related effects (frequency seizures, ASM side effects, and brain pathology) and psychosocial aspects (stigma, poor self-efficacy, low self-esteem, and teacher and parental expectations). In line with previous study [46], we assume that the fear of having a seizure in public and the stigma associated with the condition might cause social isolations, discouraging persons with epilepsy from participating fully in social activities. Reduced opportunities for social interaction might limit the experiences capable of promoting culture, referred to as not only the level of education achieved or years of schooling but also the complex of general information and knowledge, shared values, lifestyle, and behaviors in a given historical and geographical context [47].

To our knowledge, this is the first study to conduct extensive SC assessment in adult persons with IGE and

Table 5: Statistical value (p value < 0.02) of the Spearman rank correlation.

	C-TLE Seizure frequency	C-TLE Chronological age	C-TLE Years of schooling	IGE Seizure frequency	IGE Chronological age	IGE Years of schooling
Faux Pas Test						
Exclusion of nonfaux pas	0.91	0.78	0.35	0.88	0.65	0.45
Recognition on faux pas	0.022	0.003*	0.54	0.31	0.58	0.91
First question	0.028	0.001*	0.96	0.22	0.29	0.88
Second question	0.020*	0.018*	0.42	0.15	0.50	0.51
Third question	0.55	0.87	0.15	0.30	0.93	0.87
Fourth question	0.028	0.92	0.90	0.67	0.93	0.68
Total comprehension	0.88	0.11	0.59	0.80	0.50	0.98
Social Situation Test						
Normative behaviors	0.50	0.14	0.60	0.56	0.52	0.014*
Violations	0.87	0.80	0.33	0.57	0.78	0.60
Severity of violations	0.57	0.57	0.85	0.72	0.67	0.54
Moral/Conventional Distinction Test						
Recognition of moral rules	0.15	0.52	0.25	0.57	0.48	0.53
Recognition of the severity of disregard of moral rules	0.68	0.84	0.59	0.79	0.018*	0.97
Recognition of moral rules in the absence of expressed norms	0.83	0.56	0.88	0.95	0.95	0.36
Recognition of conventional rules	0.99	0.35	0.66	0.34	0.99	0.30
Recognition of the severity of disregard of conventional rules	0.49	0.64	0.18	0.99	0.32	0.82
Recognition of conventional rules in the absence of expressed norms	0.46	0.90	0.14	0.1	0.17	0.53
Empathy Questionnaire	0.23	0.68	0.58		0.92	0.48

Symbol "*" marks significant correlations ($p \leq 0.02$).

cryptoTLE and to compare their performance. Our results, although interpreted with caution, shed new light on SC impairments and on the relationship between seizures and SC impairments, contributing to a growing understanding of the complexity of epilepsy. Furthermore, the ability of ToM deficits, as expressed by FPT, to predict epilepsy group membership could have clinical diagnostic implications. SC allows us to elaborate mental representations of social relationships and use them appropriately in a social environment contributing to success of human relationships and affecting quality of life. According to this, our study findings support the integration of SC assessment in the standard neuropsychological battery of persons with epilepsy. Investigating SC is important for clinical care; knowledge of the type and severity of SC impairments might contribute to characterizing the neurobehavioral consequences of specific epilepsy syndromes as well as planning nonpharmacological treatments for alleviating psychobehavioral distress and social maladjustment.

Results of the present study should take into account some limitations. First, sample size has prevented more detailed statistical analysis; however, the participant groups were homogeneous in number, and demographic aspects and significance levels were set for between-group comparisons and correlations. Second, different types of IGE syndromes have not been analyzed although different IGE subgroups might obtain different results in SC; larger patient groups will be evaluated in future studies to clarify this point. Third, this investigation lacked a structured assessment of autism spectrum disorders that could negatively influence patients' performance on the measures of SC and EF. This limitation was compensated by detailed clinical assessment.

Another limitation of the study is lack of a standardized analysis of executive function (as attention, working memory), and these aspects could be further explored in future studies.

Fourth, correlation analysis cannot determine the direction of the effect. As linear regression analysis is not allowed by sample size, logistic regression has been applied to try explanation related to causation.

To conclude, cryptoTLE appears to be linked to more deficits in SC domains than IGE, although impaired ToM appears a distinctive feature of both conditions. While it is known that brain lesions in key areas appear to be a causative factors of SC impairment, this work suggests that the pathophysiological alterations, which could be due to seizures, could also be associated with significant SC deficits.

Data Availability

Collected data are available at IRCCS Istituto Neurologico Carlo Besta, Milano. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval

The study was approved by the Institutional Review Board and Ethics Committee of the coordinating epilepsy center Fondazione IRCCS Istituto Neurologico Carlo Besta and local review boards of participating centers. All of the research procedures were conducted in accord with the Helsinki Declaration of 1975.

Consent

The subjects gave their informed consent to the clinical and instrumental evaluations.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

GM Tallarita was responsible for the neuropsychological assessment, data analysis and interpretation, and writing the manuscript. R Ciuffini, GM Tallarita, K Turner, B Pucci, and A Parente were responsible for the patients' selection, neuropsychological assessment, and reviewing the manuscript. AR Giovagnoli was responsible for the study concept/design, data analysis and interpretation, and reviewing the manuscript.

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