Theory of Mind and Empathy in Adults With Epilepsy: A Meta-Analysis

HongZhou Wang1, PanWen Zhao2, Jing Zhao2, JianGuo Zhong3, PingLei Pan2,3, GenDi Wang2† and ZhongQuan Yi2*†

1 Department of Neurology, Anting Hospital, Shanghai, China, 2 Department of Central Laboratory, Yancheng Third People’s Hospital, The Sixth Affiliated Hospital of Nantong University, Yancheng, China, 3 Department of Neurology, Yancheng Third People’s Hospital, The Sixth Affiliated Hospital of Nantong University, Yancheng, China

Mounting evidence suggests that social cognitive abilities [including theory of mind (ToM) and empathy] are impaired in adult patients with epilepsy. Although the deficits in overall ToM in epilepsy have been documented well, the effects of epilepsy on empathic ability and specific subcomponents of ToM remain unclear. The primary aim of this study was to provide the first meta-analytic integration of ToM and empathy in adult patients with epilepsy, and to decompose these constructs to clearly differentiate their distinct (cognitive ToM and affective empathy) and overlapping (affective ToM/cognitive empathy) components. This meta-analysis included 28 studies. Adult patients with temporal lobe epilepsy (TLE) and frontal lobe epilepsy (FLE) showed impairments in cognitive ToM and affective ToM/cognitive empathy compared to the healthy controls (HCs); no group differences were identified for affective empathy. Besides, cognitive ToM was impaired in adult patients with idiopathic generalized epilepsy (IGE) and focal seizures (caused by epileptogenic foci) outside the temporal and frontal lobes (extra-TLE/FLE) and no group differences were evident for affective ToM/cognitive empathy compared to the HCs. Moreover, relative to the HCs, no group differences were identified for affective empathy in adult patients with IGE. Additionally, no (statistically) significant difference was observed between the magnitude of ToM/empathy impairment in adult patients who underwent and those who did not undergo epilepsy surgery. These quantitative findings suggest differential impairment of the core aspects of social cognitive processing in adult patients with epilepsy, which may contribute to the development of structured cognitive interventions (i.e., social cognitive training) for adult patients with epilepsy.

Keywords: theory of mind, empathy, epilepsy, meta-analysis, cognitive, affective

INTRODUCTION

Epilepsy, one of the most common neurological disorders, affects over 50 million people worldwide (1). It is characterized by chronic, unprovoked, and recurrent seizures (2). Epilepsy is usually complicated by numerous neurobiological disorders, cognitive impairment, and psychosocial ramifications, which lead to a severe economic burden and deterioration in the quality of life (1–5).
Cognitive impairment, including memory impairment, language dysfunction, attention deficit, executive dysfunction, and social cognitive impairment, is considered to be a common symptom of epilepsy (6–14). According to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (15), social cognition is a core neurocognitive domain, which is defined as the ability to understand and predict the behavior of others based on their beliefs, feelings and intentions, and interact in complex social environments and relationships (16–20). Social cognition is a multidimensional construct that mainly involves theory of mind (ToM), empathy, social perception and knowledge, and attribution bias (21–23).

ToM is, in turn, a core domain of social cognition, which denotes the ability to understand and act according to the mental states (beliefs, intentions, and desires) of other humans (24–26). ToM is a complex ability that encompasses multiple components, mainly the cognitive and affective domains (27). Cognitive ToM refers to the ability to derive inferences about the thoughts, intentions, beliefs, and motivations of others, while affective ToM is the ability to infer others’ feelings, affective states, and emotions (28, 29).

Empathy, another core aspect of social cognition, refers to the ability to understand and feel another's emotions and to respond appropriately and with compassion (30–35). Empathy, akin to ToM, is also a complex and multifaceted phenomenon, which mainly comprises the cognitive and affective dimensions (36). Cognitive empathy is the ability to understand the thoughts and emotions of others, while affective empathy confers the ability to feel and share the emotions of another the emotional state of others (37–41).

Notably, although conceptually there are differences between affective ToM and cognitive empathy, these two constructs are difficult to distinguish at the level of purely behavioral assessment (42–50). Furthermore, the overlap between affective ToM and cognitive empathy is frequently noted (42–44, 46, 50). Specifically, they both involve attributions to emotional state of others. Therefore, we use the terms affective ToM and cognitive empathy interchangeably herein.

Although numerous recent studies have assessed ToM and empathy deficits in adult patients with epilepsy, their conclusions have been inconsistent (51–55), which may be attributed to low statistical power, since a majority of these studies enrolled small patient populations (56–59). A quantitative meta-analysis may improve the statistical power, estimate the severity of these deficits, and refine the conclusions drawn from the inconsistent findings of previous studies (20).

To the best of our knowledge, no meta-analysis has investigated empathy deficits in adult patients with epilepsy. Although two meta-analyses examined the differences in ToM between patients with epilepsy and HCs (11, 13), no previous meta-analysis has investigated the differences between cognitive ToM and affective ToM in adult patients with epilepsy. Moreover, the two above-mentioned meta-analyses only included studies that investigated five specific ToM tasks (faux-pas task, false belief tasks, reading the mind in the eyes task, strange stories task, and cartoon ToM task), and some other important ToM tasks were not included (such as the Yoni task and the movie task).

METHODS

Study Registration
This meta-analysis protocol was registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (ID: INPLASY 2021120039).

Literature Search Strategy and Data Sources
This meta-analysis was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (60). Databases including Web of Science, PubMed, and Embase were searched on November 20, 2021 using the following search terms: ["epilepsy" or "seizure disorder"] AND ["social cognition" or "theory of mind" or "ToM" or "mentaling" or "mentalizing" or "empathy" or "perspective taking"]. Furthermore, other resources, such as the reference lists for the assessment of social cognition). Additionally, both previous meta-analysis included patients from different age groups. Furthermore, Bora and Meletti (11) investigated ToM deficits in temporal lobe epilepsy (TLE). Although Stewart et al. (13) investigated ToM impairment in different types of epilepsy [TLE, frontal lobe epilepsy (FLE), idiopathic generalized epilepsy (IGE), and focal seizures outside the temporal and frontal lobes (extra-TLE/FLE)], they included only two studies to investigate ToM impairment in patients with IGE and extra-TLE/FLE, and three studies to investigate ToM impairment in patients with FLE, owing to limitations of the other available studies.

Therefore, the primary aim of this study was to provide the first meta-analytic integration of ToM and empathy in adult patients with epilepsy and investigate the cognitive and affective subcomponents of these two entities. Specific subgroup analyses were conducted to evince a clear differentiation between the separate components (cognitive ToM and affective empathy) and overlapping components (affective ToM/cognitive empathy).

Furthermore, subgroup analyses were performed to assess whether the deficits in ToM and empathy were related to the site of the epileptogenic focus (including TLE, FLE, IGE, and extra-TLE/FLE), considering that epileptic seizures are categorized by seizure onset into focal, generalized, combined generalized, and focal, and unknown (1). Moreover, subgroup analyses were conducted in adult patients with TLE who underwent and those who did not undergo epilepsy surgery [pre-surgical studies (TLE-TL-) and post-surgical studies (TLE-TL +)], to investigate whether temporal lobectomy is related to ToM and empathy deficits in adult patients with TLE. Furthermore, we evaluated the effect of potential variables such as mean age, sex (ratio of female patients in the epilepsy group), education level, age of epilepsy onset, disease duration, monthly seizure frequency, number of anti-epileptic drugs (AEDs) administered, and intelligence quotient (IQ) scores on social cognition. We hope that this meta-analysis will provide a more comprehensive and nuanced understanding of the effect of epilepsy on ToM and empathy in adults with epilepsy.
of all included studies, were searched to identify studies that were not indexed in these databases.

**Inclusion Criteria**
The inclusion criteria for this review were as follows: (1) studies published in English in peer-reviewed journals, (2) studies that used measures to assess at least one domain of ToM or empathy performance, (3) studies comparing ToM or empathy performance between adult patients with epilepsy and HCs, and (4) studies that reported adequate data to calculate the effect sizes of ToM or empathy.

**Exclusion Criteria**
Studies were excluded for the following reasons: (1) absence of comparisons of ToM or empathy between patients with epilepsy and HCs, (2) the study sample overlapped with another study with a larger sample size, (3) studies that grouped patients with different sites of epileptogenic foci together, and (4) studies whose a sample size was less than 10 (26).

**Study Quality Assessment**
A nine-star protocol was used to assess study quality, based on the Newcastle-Ottawa Scale. The study was considered to be of high quality if the star rating was ≥ 7 (61).

**Screening and Data Extraction**
Two investigators independently completed article retrieval, screening, data extraction, and quality evaluation. The following data were extracted: (a) title information, such as the name of the first author, year of publication, and title; (b) sample characteristics, such as the number of participants in the epilepsy and control groups, mean age, sex (female and male patients), epilepsy type, monthly seizure frequency, whether surgery was performed or not, number of AEDs, education level, disease duration, and IQ score; (c) the tasks were divided into the cognitive and affective subcomponents for both ToM and empathy; and (d) the data were used to calculate the mean effect sizes of ToM or empathy.

**Statistical Analysis**
Data were analyzed using Stata 15.0 with a random-effects model (62). Hedges g and 95% confidence intervals (CIs) were calculated to estimate differences in ToM and empathy between adult patients with epilepsy and HCs (63). The interpretation of Hedges g was similar to that of Cohen d: 0.2 indicated a small effect, 0.5 indicated a medium effect, and 0.8 indicated a large effect (64). Negative effect sizes indicated poorer performance of the adult patients with epilepsy compared to the HCs.

When studies did not provide a total mean score on a particular measure (i.e., overall ToM, overall empathy, cognitive ToM, affective empathy, and affective ToM/cognitive empathy), but reported more than one ToM or empathy task, a pooled effect size was aggregated by computing the mean effect size (and standard error) (65). The heterogeneity of the mean weighted effect sizes across analyses was tested using the $I^2$ test, and the degree of heterogeneity was deemed low, moderate, or large.

---

**FIGURE 1** | Flow diagram of identification and selection of studies.
when the value of $I^2$ was equal to or larger than 0, 50, or 75%, respectively (66). Publication bias was assessed using funnel plots and Egger’s test (67). If publication bias was found, the trim-and-fill method was applied to obtain effect sizes adjusted for publication bias (68).

Meta-regression analyses were conducted for age, sex, education level, age at epilepsy onset, disease duration, monthly seizure frequency, number of AEDs, and IQ scores. A minimum of 10 data points was required for each relevant predictor variable and the social cognitive ability under assessment for each of these analyses (69).

Notably, since we used the terms affective ToM and cognitive empathy interchangeably in this paper, we defaulted that the data of affective ToM/cognitive empathy is the same as the data of affective ToM or cognitive empathy.

RESULTS

Study Characteristics

The details of the study selection process are depicted in Figure 1. Initially, 2418 articles were retrieved from three databases (Web of Science, PubMed, and Embase) and one article was retrieved from other sources. After eliminating duplicate studies, 1905 articles remained, which were then subjected to title and abstract screening. Subsequently, 62 full text papers were reviewed. Thirty-four of the 62 studies were excluded for the following reasons: the sample size was under 10 ($K = 1$) (70), the sample was mixed and included patients with epilepsy and other diseases ($K = 1$) (71); patients with different sites of the epileptogenic focus were grouped together ($K = 1$) (25); the samples overlapped with those of other studies ($K = 4$) (52, 72–74); the study did not include an HC group ($K = 5$) (75–79); data were insufficient to calculate the effect sizes and standard errors of ToM or empathy ($K = 6$) (80–85); and the study population included children or adolescents ($K = 16$) (51, 53, 55, 59, 86–97). Eventually, 28 studies were included in the meta-analysis (Table 1) (54, 56–58, 98–121).

The studies included 902 adult patients with TLE (21 studies), 205 adult patients with FLE (6 studies), 128 adult patients with IGE (5 studies), and 70 adult patients with extra-TLE/FLE (3 studies).

The results of the assessment of study quality are presented in Table 2, and the mean score was 6.86 ($SD = 0.79$). Nineteen of the 28 case-control studies were awarded ≥ 7 stars and considered to be of high quality.

Theory of Mind and Empathy in Adult Patients With Frontal Lobe Epilepsy vs. Healthy Controls

The key results from this meta-analysis are presented in Table 4. Adult patients with FLE exhibited significant impairment in overall ToM ($g = -0.93, 95\% CI (-1.28, -0.57), K = 6$; Figure 4) and overall empathy ($g = -0.94, 95\% CI (-1.36, -0.53), K = 6$; Figure 4) compared to the HCs. The examination of the overlapping and distinct subcomponents of these constructs revealed associations between adult patients with FLE and severe deficits in cognitive ToM ($g = -1.06, 95\% CI (-1.31, -0.80), K = 4$; Figure 4) and affective ToM/cognitive empathy ($g = -0.96, 95\% CI (-1.40, -0.51), K = 6$; Figure 4). However, no group differences were evident for affective empathy ($g = -0.31, 95\% CI (-0.67, 0.05), K = 1$; Figure 4). There was no heterogeneity across studies for affective empathy ($I^2 = 0$) and moderate heterogeneity for cognitive ToM ($I^2 = 65\%$), but a significant variation was observed for overall ToM ($I^2 = 85\%$), overall empathy ($I^2 = 84\%$), and affective ToM/cognitive empathy ($I^2 = 77\%$). Egger’s test did not reveal significant publication bias for overall ToM, overall empathy, cognitive ToM, affective ToM/cognitive empathy, or affective empathy.

Theory of Mind and Empathy in Adult Patients With Idiopathic Generalized Epilepsy vs. Healthy Controls

The key results from this meta-analysis are shown in Table 5. Adult patients with IGE exhibited mild deficits in overall ToM ($g = -0.42, 95\% CI (-0.58, -0.27), K = 5$; Figure 5) and cognitive ToM ($g = -0.498, 95\% CI (-0.77, -0.23), K = 4$; Figure 5) compared to the HCs. However, no group differences were evident for overall empathy ($g = -0.36, 95\% CI (-0.74, 0.02), K = 4$; Figure 5), affective ToM/cognitive empathy ($g = -0.33, 95\% CI (-0.69, 0.04), K = 4$; Figure 5), and affective empathy ($g = -0.24, 95\% CI (-0.86, 0.38), K = 1$; Figure 5). There was no heterogeneity across studies for affective empathy ($I^2 = 0$), small heterogeneity for overall ToM ($I^2 = 16\%$), cognitive ToM ($I^2 = 48\%$), affective ToM/cognitive empathy ($I^2 = 46\%$), and moderate heterogeneity for overall empathy ($I^2 = 51\%$). Egger’s test did not reveal significant publication bias for overall ToM, overall empathy, cognitive ToM, or affective ToM/cognitive empathy.
| References                | Groups (female) | Age (years, SD) | Education (years, SD) | Mean age at onset (years, SD) | Duration (years, SD) | Monthly seizure frequency (SD) | Number of AEDS (SD) | Surgical status | Task | Type              |
|---------------------------|-----------------|-----------------|-----------------------|-----------------------------|----------------------|-------------------------------|-------------------|-----------------|------|-------------------|
| Amlerova et al. (105)     | TLE = 74 (29)   | 35.78 (9.94)    | NA                    | 18.28 (12.23)               | NA                   | 7.19 (7.66)                   | NA                | Pre + post      | FPT  | CogToM            |
|                           | HCs = 20 (14)   | 33.00 (13.00)   | NA                    | 12.22 (9.91)               | 21.47 (10.86)        | 8.05 (10.41)                   | NA                | Frith-Happé animations | Mixed ToM |
| Bala et al. (114)         | TLE = 40 (21)   | 34.44 (8.51)    | 13.46 (2.83)          | 12.22 (1.51)               | 21.47 (10.86)        | 8.05 (10.41)                   | NA                | Pre + post      | FPT  | AffTom/CogEmp     |
|                           | HCs = 20 (10)   | 30.23 (11.49)   | 16.00 (5.14)          | NA                         | 22.16 (15.6)         | NA                           | NA                | Mixed ToM       | Mixed ToM |
| Bauer et al. (116)        | TLE = 17 (8)    | 38.20 (14.80)   | NA                    | 14.73 (13.12)              | NA                   | NA                           | NA                | Post            | RMET | CogToM            |
|                           | HCs = 51 (26)   | 36.80 (10.90)   | NA                    | NA                         | NA                   | NA                           | NA                | AffEmp          | Mixed ToM |
|                          |                 |                 |                       |                            |                      |                               |                   |                 |                  |                   |
| Boucher et al. (57)       | TLE = 15 (8)    | 38.70 (10.30)   | 13.30 (2.80)          | 14.73 (13.12)              | NA                   | NA                           | NA                | Post            | RMET | CogToM            |
|                           | HCs = 20 (10)   | 36.10 (10.20)   | 13.50 (1.80)          | NA                         | NA                   | NA                           | NA                | AffEmp          | Mixed ToM |
| Brocher et al. (102)      | TLE = 28 (16)   | 34.43 (13.25)   | 13.82 (3.56)          | 20.21                      | 14.25                | NA                           | NA                | Pre             | RMET | AffTom/CogEmp     |
| Extra-TLE/FLE = 14 (10)   |                 | 33.36 (11.74)   | 14.04 (2.41)          | 18.57                      | 14.76                | NA                           | NA                | Moving Triangles | CogToM |
|                           | HCs = 29 (16)   | 33.69 (10.94)   | 14.03 (2.86)          | NA                         | NA                   | NA                           | NA                | FPT—affective attributions | AffTom/CogEmp |
|                           |                 |                 |                       |                            |                      |                               |                   | FPT—epistemic attributions | AffTom/CogEmp |
| Cohn et al. (106)         | TLE = 87 (42)   | 39.38 (12.14)   | 14.50 (2.83)          | 16.7                       | NA                   | NA                           | NA                | Pre + Post      | TASIT—SIM       | Mixed ToM |
|                           | HCs = 15 (10)   | 38.30 (8.60)    | 15.60 (2.70)          | NA                         | NA                   | NA                           | NA                | Mixed ToM       | Mixed ToM |
| Farrant et al. (99)       | FLE = 14 (8)    | 34.36 (12.50)   | 11.93 (0.73)          | 11.8                       | NA                   | NA                           | NA                | FPT—Researchers | RMET | CogToM            |
|                           | HCs = 14 (8)    | 35.79 (9.91)    | 11.50 (0.65)          | NA                         | NA                   | NA                           | NA                | Cartoon ToM    | Mixed ToM |
|                          |                 |                 |                       |                            |                      |                               |                   | Strange stories task | CogToM |
| Giorgi et al. (110)       | IGE = 20 (18)   | 26.70 (6.60)    | 14.60 (2.50)          | 14                         | 12.7                  | NA                           | NA                | Pre             | RMET | CogToM            |
|                           | HCs = 20 (18)   | 26.20 (8.80)    | 15.20 (2.50)          | NA                         | NA                   | NA                           | NA                | FPT             | CogToM |
| Giovagnoli et al. (101)   | TLE = 109 (65)  | 36.83 (11.25)   | 11.79 (3.65)          | 21.33                      | 15.49                 | 9.11                          | 2.07              | Pre             | RMET | AffTom/CogEmp     |
|                           | FLE = 29 (18)   | 35.77 (12.53)   | 12.40 (3.34)          | 26.07                      | 13.94                 | 8.91                          | 1.91              | FPT             | CogToM |
|                           | HCs = 49 (40)   | 52.03 (17.04)   | 11.38 (3.81)          | NA                         | NA                   | NA                           | NA                | FPT             | CogToM |
| Giovagnoli et al. (103)   | TLE = 54 (28)   | 37.80 (9.20)    | 11.91 (3.47)          | 18.7                       | 18.89                 | 9.33                          | 2.13              | Pre             | RMET | CogToM            |
|                           | FLE = 12 (6)    | 37.17 (13.41)   | 11.25 (3.25)          | 25.33                      | 11.83                 | 14.73                         | 2.09              | FPT             | CogToM |
|                           | HCs = 42 (24)   | 40.64 (12.61)   | 11.81 (3.38)          | NA                         | NA                   | NA                           | NA                | FPT             | CogToM |
| Giovagnoli et al. (111)   | TLE = 85 (33)   | 33.80 (9.99)    | 11.62 (3.44)          | 17.22 (11.21)              | 16.68 (11.71)        | 8.86 (11.90)                   | 2.24 (0.91)       | Pre + post      | RMET | AffTom/CogEmp     |
|                           | HCs = 40 (11)   | 36.50 (9.64)    | 12.20 (3.16)          | NA                         | NA                   | NA                           | NA                | FPT             | CogToM |

(Continued)
| References                      | Groups (female) | Age (years, SD) | Education (years, SD) | Mean age at onset (years, SD) | Duration (years, SD) | Monthly seizure frequency (SD) | Number of AEDS (SD) | Surgical status | Task                              | Type                   |
|--------------------------------|-----------------|-----------------|-----------------------|-------------------------------|----------------------|-------------------------------|-------------------|----------------|-----------------------------------|------------------------|
| Giovagnoli et al. (118)        | FLE = 75 (30)   | 35.49 (11.19)   | 12.37 (3.29)          | 22.03 (14.14)                 | 13 (11.6)            | 6.26 (0.98)                   | 1.97 (0.88)       |                | FPT                              | CogToM                 |
| HCs = 42 (16)                  |                 | 44.93 (14.65)   | 12.33 (3.21)          |                              |                      |                              |                   |                |                                   |                        |
| Giovagnoli et al. (120)        | TLE = 50 (31)   | 40.08 (12.98)   | 12.14 (2.96)          | 23.22 (13.49)                 | 16.46 (12.29)        | 4.52 (11.96)                  | 1.76 (0.8)        | Pre            | FPT                              | CogToM                 |
| HCs = 50 (29)                  |                 | 39.20 (13.32)   | 14.86 (3.22)          |                              |                      |                              |                   |                |                                   |                        |
| Gu and Ahmad (54)              | FLE = 60 (30)   | 28.70 (1.39)    | 12.83 (1.36)          | 13.23 (1.78)                  | NA                   | NA                           | NA                |                | iRI—cognitive empathy             | AffTom/CogEmp          |
| HCs = 60 (30)                  |                 | 28.83 (1.98)    | 12.76 (1.25)          |                              |                      |                              |                   |                | iRI—affective empathy             | AffEmp                 |
| Gürgoy et al. (119)            | IGE = 28 (19)   | 34.04 (8.88)    | 10.21 (3.28)          | 19.64 (1.76)                  | 14.93 (9.95)         | NA                           | NA                |                | RMET                             | AffTom/CogEmp          |
| HCs = 28 (20)                  |                 | 35.11 (7.19)    | 10.32 (3.56)          |                              |                      |                              |                   |                |                                   |                        |
| Hennion et al. (107)           | TLE = 50 (27)   | 42.40 (11.82)   | NA                    | 21.06 (15.27)                 | 21.34 (14.59)        | 13.2 (63.6)                  | NA                | Pre            | The comprehension of sarcasm task | Mixed ToM              |
| HCs = 50 (27)                  |                 | 42.81 (12.46)   | NA                    |                              |                      |                              |                   |                |                                   |                        |
| Hennion et al. (58)            | TLE = 25 (11)   | 42.32 (10.91)   | 17.56 (13.08)         | 24.28 (13.98)                 | 3.64 (6.63)          | 2.04 (0.68)                  |                   |                | FPT                              | CogToM                 |
| HCs = 25 (11)                  |                 | 42.50 (12.30)   | NA                    |                              |                      |                              |                   |                |                                   |                        |
| Jasionis et al. (121)          | IGE = 27 (22)   | 27.01 (6.01)    | 13.75 (2.00)          | NA                           | 11.67 (7.67)         | NA                           | NA                |                | The animated shapes task          | Mixed ToM              |
| Extra-TLE/FLE = 29 (16)        |                 | 33.03 (11.60)   | 13.61 (3.21)          | NA                           | 16.86 (9.27)         | NA                           | NA                |                |                                   |                        |
| Javor et al. (117)             | FLE = 15 (8)    | 36.00 (8.10)    | NA                    | NA                           | NA                   | NA                           | NA                |                | RMET                             | AffTom/CogEmp          |
| HCs = 15 (8)                   |                 | 34.07 (6.05)    | NA                    | NA                           | NA                   | NA                           | NA                |                | False Belief test                 | CogToM                 |
| Li et al. (104)                | TLE = 31 (13)   | 41.91 (13.20)   | 14.03 (2.75)          | 24.45 (13.45)                 | 18.55 (13.19)        | 1.29 (1.20)                  | 2.02 (1.17)       | Pre            | FPT                              | CogToM                 |
| HCs = 24 (11)                  |                 | 37.75 (16.77)   | 14.29 (2.97)          |                              |                      |                              |                   |                | Implication Stories test          | CogToM                 |
| Morou et al. (115)             | IGE = 35 (27)   | 29.90 (11.50)   | 12.66 (3.25)          | 17.28 (7.59)                  | NA                   | NA                           | 1.64 (1.27)       |                | Cartoon ToM                       | CogToM                 |
| HCs = 70 (27)                  |                 | 32.60 (10.99)   | 12.48 (2.29)          |                              |                      |                              |                   |                | Hinting Task                      | CogToM                 |

(Continued)
### TABLE 1 (Continued)

| References | Groups (female) | Age (years, SD) | Education (years, SD) | Mean age at onset (years, SD) | Duration (years, SD) | Monthly seizure frequency (SD) | Number of AEDS (SD) | Surgical status | Task | Type |
|------------|----------------|----------------|----------------------|-------------------------------|---------------------|-------------------------------|-------------------|----------------|------|------|
| Okruszek et al. (112) | TLE = 40 (21) | 34.44 (9.51) | 13.46 (2.83) | 12.22 (9.91) | 21.47 (10.86) | 8.05 (10.41) | NA | Pre + Post | sarcasm and metaphor |
| HCs = 20 (10) | 30.23 (11.49) | 16.00 (1.51) | 12 (NA) | NA | 23 (NA) | NA | Pre | CogToM |
| Okruszek et al. (113) | TLE = 31 (17) | 30.90 (7.70) | 13.00 (2.90) | 12 (NA) | NA | 1.3 (0.7) | Pre | RMET | AffTom/CogEmp |
| HCs = 47 (22) | 32.30 (9.10) | 15.90 (1.80) | 15.00 (9.10) | 14.00 (2.90) | 22.0 (13.2) | 12.9 (10) | NA | Pre | RMET | AffTom/CogEmp |
| Realmuto et al. (108) | TLE = 21 (13) | 37.00 (12.50) | 10.80 (3.10) | 24.3 (13.2) | 12.9 (10) | NA | 1.3 (0.7) | Pre | RMET | AffTom/CogEmp |
| IGE = 18 (12) | 26.30 (7.20) | 11.90 (2.60) | 15.14 (7.7) | 13.5 (8.2) | 1.2 (0.5) | SET—emotion attribution | AffEmp |
| HCs = 21 (9) | 31.95 (11.54) | 12.50 (3.96) | 13.3 (11.4) | 22.2 (13.8) | NA | NA | Pre + Post | FPT | CogToM |
| Schacher et al. (100) | TLE = 27 (14) | 36.50 (10.70) | NA | 15.6 (14.5) | 20.3 (15.1) | NA | NA | Pre + Post | FPT | CogToM |
| Extra-TLE/FLE = 27 (1) | 35.90 (12.80) | NA | 14.12 (9.73) | NA | NA | NA | Post | FPT | CogToM |
| HCs = 12 (9) | 33.80 (12.40) | NA | 14.12 (9.73) | NA | NA | NA | Post | False Belief test | CogToM |
| HCs = 38 (21) | 36.00 (11.00) | NA | 26 (14.25) | NA | NA | Pre + Post | Strange Stories task | CogToM |
| Shaw et al. (56) | TLE = 19 (11) | 37.21 (10.54) | NA | NA | 26 (14.25) | NA | NA | Pre + Post | Strange Stories task | CogToM |
| HCs = 19 (13) | 33.00 (11.00) | NA | 13.88 (2.48) | 18.51 (11.19) | 13.72 (9.59) | 3.22 (5.88) | 2.61 (0.73) | Pre | FPT | CogToM |
| Wang et al. (109) | TLE = 67 (31) | 32.19 (10.22) | 13.88 (2.48) | 18.51 (11.19) | 13.72 (9.59) | 3.22 (5.88) | 2.61 (0.73) | Pre | FPT | CogToM |
| HCs = 30 (14) | 33.40 (9.57) | 14.33 (2.11) | 13.88 (2.48) | 18.51 (11.19) | 13.72 (9.59) | 3.22 (5.88) | 2.61 (0.73) | Pre | FPT | CogToM |

SD, standard deviation; NA, not available; AEDS, antiepileptic drugs; TLE, temporal lobe epilepsy; FLE, frontal lobe epilepsy; IGE, idiopathic generalized epilepsy; extra-TLE/FLE, local seizures (caused by epileptogenic foci) outside the temporal and frontal lobes; HCs, healthy controls; ToM, theory of mind; EMP, empathy; CogToM, Cognitive ToM; AffToM/CogEmp, Affective ToM/Cognitive empathy; AffEmp, Affective empathy; FPT, Faux pas task; MASC, the Movie for the Assessment of Social Cognition; IRI, Interpersonal Reactivity Index; TASIT, the Awareness of Social Inference Test; SIM, Social Inference-Minimal Test; SIE, Social Inference-Enriched; RMET, Reading the Mind in the Eyes Test; SET, Story-based Empathy Task.
Table 2 | Quality evaluation of included studies.

| References                        | S1 | S2 | S3 | S4 | C | E1 | E2 | E3 | Sum |
|-----------------------------------|----|----|----|----|---|----|----|----|-----|
| Amlerova et al. (105)             | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 6   |
| Bala et al. (114)                 | ✧  | —  | ✧  | —  | — | ✧  | —  | —  | 7   |
| Bauer et al. (116)                | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Boucher et al. (57)               | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Broicher et al. (130)             | ✧  | ✧  | —  | —  | — | ✧  | —  | —  | 8   |
| Cohn et al. (106)                 | ✧  | —  | ✧  | —  | — | ✧  | —  | —  | 6   |
| Farrant et al. (99)               | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Giorgi et al. (110)               | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Giovagnoli et al. (101)           | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 6   |
| Giovagnoli et al. (103)           | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Giovagnoli et al. (111)           | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Giovagnoli et al. (118)           | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Giovagnoli et al. (120)           | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 6   |
| Gul and Ahmad (54)                | ✧  | ✧  | ✧  | —  | — | ✧  | —  | —  | 9   |
| Guşşy et al. (119)                | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 8   |
| Hennon et al. (52) and Hennon et al. (107) | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 8   |
| Hennon et al. (58)                | ✧  | —  | ✧  | ✧  | — | ✧  | —  | —  | 8   |
| Jasionis et al. (121)             | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 6   |
| Javor et al. (117)                | ✧  | —  | ✧  | —  | — | ✧  | —  | —  | 6   |
| Li et al. (104)                   | ✧  | —  | ✧  | ✧  | — | ✧  | —  | —  | 7   |
| Morou et al. (115)                | ✧  | —  | ✧  | ✧  | — | ✧  | —  | —  | 7   |
| Okruszek et al. (112)             | ✧  | —  | —  | ✧  | — | ✧  | —  | —  | 6   |
| Okruszek et al. (113)             | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Realmuto et al. (108)             | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 8   |
| Schacher et al. (100)             | ✧  | ✧  | —  | ✧  | — | ✧  | —  | —  | 7   |
| Shaw et al. (56)                  | ✧  | —  | ✧  | ✧  | — | ✧  | —  | —  | 6   |
| Shaw et al. (56)                  | ✧  | —  | ✧  | ✧  | — | ✧  | —  | —  | 6   |
| Wang et al. (109)                 | ✧  | —  | ✧  | ✧  | — | ✧  | —  | —  | 7   |

We herein selected “age” as the most important adjusting factor and selected “sex” as other controlled factor. S1, Is the case definition adequate? S2, Representativeness of the cases; S3, Selection of Controls; S4, Definition of Controls; C, Comparability of cases and controls on the basis of the design or analysis; E1, Ascertainment of exposure; E2, Same method of ascertainment for cases and controls; E3, Non-response rate.

Table 3 | Mean effects for ToM and empathy subcomponents comparing participants with TLE against healthy controls and tests for publication bias.

| Subcomponent | K | N in TLE groups | N in HCs groups | g | 95% CI | Test for Heterogeneity | Assess risk of publication bias |
|--------------|---|-----------------|-----------------|---|--------|------------------------|-------------------------------|
| Overall ToM  | 21| 921             | 672             | −0.91| −1.05 | 0.77 | 66 | 0.067 | No change |
| Overall empathy | 11| 509             | 466             | −0.71| −0.89 | 0.52 | 52 | 0.885 | No change |
| CogToM       | 15| 887             | 529             | −0.91| −1.10 | 0.72 | 78 | 0.187 | No change |
| AffToM/CogEmp| 11| 509             | 466             | −0.76| −0.88 | 0.63 | 0  | 0.662 | No change |
| AffEmp       | 3 | 86              | 91              | −0.16| −0.49 | 0.17 | 29 | 0.275 | No change |

TLE, temporal lobe epilepsy; HCs, healthy controls; CI, confidence interval; CogToM, cognitive ToM; AffToM/CogEmp, affective ToM/cognitive empathy; AffEmp, affective empathy; g, Hedges g; K, the number of studies; N, the number. Trim and fill: look for missing studies to left of mean; using random effects model. Imputed mean is random effects.

Theory of Mind and Empathy in Adult Patients With Extra-Temporal Lobe Epilepsy/Frontal Lobe Epilepsy vs. Healthy Controls

The key results obtained from this meta-analysis are depicted in Table 6. Adult patients with extra-TLE/FLE showed mild deficits in overall ToM [g = −0.48, 95% CI (−0.85, −0.12), K = 3; Figure 6] and cognitive ToM [g = −0.499, 95% CI (−0.88, −0.12), K = 3; Figure 6] compared to HCs. However, no group differences were evident for overall empathy [g = −0.26, 95% CI (−0.71, 0.18), K = 1; Figure 6] and affective ToM/cognitive empathy [g = −0.26, 95% CI (−0.71, 0.18), K = 1; Figure 6]. There was no heterogeneity across studies for overall empathy (I² = 0), affective ToM/cognitive empathy (I² = 0), and little heterogeneity for overall ToM (I² = 48%) and cognitive
FIGURE 2 | Forest plots showing effect size estimates (Hedges g) for overall ToM and overall empathy differences between TLE and healthy controls. CI, confidence interval; TLE, temporal lobe epilepsy; ToM, theory of mind.

ToM ($I^2 = 44\%$). Egger’s test was not significant for overall or cognitive ToM.

ToM ($I^2 = 44\%$). Egger’s test was not significant for overall or cognitive ToM.

**Empathy and Theory of Mind in Adult Patients With Temporal Lobe Epilepsy With and Without Epilepsy Surgery vs. Healthy Controls**

Table 7 depicts the key results obtained from this meta-analysis. The performance of adult patients with TLE-TL- and TLE-TL+ with respect to overall ToM ($g = -0.89$ and $g = -0.92$), overall empathy ($g = -0.77$ and $g = -0.57$), cognitive ToM ($g = -0.89$ and $g = -0.77$), and affective ToM/cognitive empathy ($g = -0.79$ and $g = -0.65$) was inferior to that of the HCs. However, no group differences were evident for overall empathy ($g = -0.27$ and $g = -0.02$). The effect sizes of the TLE-TL- and TLE-TL+ groups were comparable for overall ToM ($Q = 0.03$, $df = 1$, $p = 0.863$), overall empathy ($Q = 0.82$, $df = 1$, $p = 0.366$), cognitive ToM ($Q = 0.34$, $df = 1$, $p = 0.56$), affective ToM/cognitive empathy ($Q = 1.01$, $df = 1$, $p = 0.314$), and affective empathy ($Q = 0.46$, $df = 1$, $p = 0.498$).

Egger’s test was not significant, except for overall ToM in adult patients with TLE-TL+. However, a trim-and-fill analysis
did not result in imputation of any studies, and the effect size remained the same.

**Meta-Regression Analyses**

Meta-regressions were not conducted for the effect of potential variables (age, sex, education level, age at epilepsy onset, disease duration, monthly seizure frequency, number of AEDs, and IQ score) on the severity of ToM/empathy in adult patients with FLE, IGE, or extra-TLE/FLE, as less than 10 studies contributed to the data for this subcomponent.

The variables (age, sex, education level, age at epilepsy onset, disease duration, and monthly seizure frequency) associated with adult patients with TLE did not account for any significant variance in overall ToM ($p = 0.871, 0.218, 0.582, 0.996, 0.712,$ and $0.318,$ respectively), overall empathy ($p = 0.871, 0.218, 0.582, 0.996, 0.712,$ and $0.318,$ respectively), cognitive ToM ($p = 0.871, 0.218, 0.582, 0.996, 0.712,$ and $0.318,$ respectively), and affective ToM/cognitive empathy ($p = 0.871, 0.218, 0.582, 0.996, 0.712,$ and $0.318,$ respectively). No meta-regressions were conducted for the variables associated with affective empathy, or for those (number of AEDs and IQ score) associated with overall ToM, overall empathy, cognitive ToM, and affective ToM/cognitive empathy, as less than 10 studies provided data for this subcomponent.
TABLE 4 | Mean effects for ToM and empathy subcomponents comparing participants with FLE against healthy controls and tests for publication bias.

| Subcomponent                  | K  | N in FLE groups | N in HCs groups | $g$    | 95% CI          | Test for Heterogeneity | Assess risk of publication bias |
|-------------------------------|----|----------------|----------------|-------|----------------|------------------------|------------------------------|
|                               |    |                |                |       | Lower | Upper | $I^2$ Statistic,\% | Egger's test P-value | Trim and fill imputed $g$ |
| Overall ToM                   | 6  | 205            | 242            | −0.93 | −1.28 | −0.57 | 85                  | 0.371                     | No change |
| Overall empathy               | 6  | 205            | 242            | −0.94 | −1.36 | −0.53 | 84                  | 0.554                     | No change |
| CogToM                        | 4  | 130            | 167            | −1.06 | −1.31 | −0.80 | 65                  | 0.599                     | No change |
| AffToM/CogEmp                | 6  | 205            | 242            | −0.96 | −1.40 | −0.51 | 77                  | 0.317                     | No change |
| AffEmp                        | 1  | 60             | 60             | −0.31 | −0.67 | 0.05  | 0                   |                           |                      |

FLE, frontal lobe epilepsy; HCs, healthy controls; ToM, theory of mind; CI, confidence interval; CogToM, cognitive ToM; AffToM/CogEmp, affective ToM/cognitive empathy; AffEmp, affective empathy; $g$, Hedges $g$; $K$, the number of studies; $N$, the number. Trim and fill: look for missing studies to left of mean; using random effects model. Imputed mean is random effects.

FIGURE 4 | Forest plots showing effect size estimates (Hedges $g$) for overall ToM, overall empathy, cognitive ToM, affective ToM/cognitive empathy, and affective empathy differences between FLE and healthy controls. CI, confidence interval; FLE, frontal lobe epilepsy; ToM, theory of mind.
TABLE 5 | Mean effects for ToM and empathy subcomponents comparing participants with IGE against healthy controls and tests for publication bias.

| Subcomponent          | K | N in IGE groups | N in HCs groups | g   | 95% CI | I² statistic, % | Test for heterogeneity | Assess risk of publication bias |
|-----------------------|---|----------------|----------------|-----|--------|----------------|------------------------|-------------------------------|
|                       |   |                |                |     | Lower  | Upper         |                        |                               |
| Overall ToM           | 5 | 128            | 169            | -0.42 | -0.58  | -0.27         | 16                     | 0.564 No change               |
| Overall empathy       | 4 | 101            | 139            | -0.36 | -0.74  | 0.02          | 51                     | 0.128 No change               |
| CogToM                | 4 | 110            | 148            | -0.498| -0.77  | -0.23         | 48                     | 0.288 No change               |
| AffToM/CogEmp         | 4 | 101            | 139            | -0.33 | -0.69  | 0.04          | 46                     | 0.170 No change               |
| AffEmp                | 1 | 18             | 21             | -0.24 | -0.86  | 0.38          | 0                      |                               |

IGE, idiopathic generalized epilepsy; HCs, healthy controls; ToM, theory of mind; CI, confidence interval; CogToM, cognitive ToM; AffToM/CogEmp, affective ToM/cognitive empathy; AffEmp, affective empathy; g, Hedges g; K, the number of studies; N, the number. Trim and fill: look for missing studies to left of mean; using random effects model. Imputed mean is random effects.

Study ID

| Hedges g (95% CI) | Weight % |
|-------------------|----------|
| Giorgi et al.2016 | -0.77 (-1.13, -0.40) | 14.86 |
| Gursoy et al.2021 | -0.24 (-0.64, 0.16)  | 12.87 |
| Jasionis et al.2021 | -0.45 (-0.82, -0.08) | 14.71 |
| Morou et al.2018  | -0.36 (-0.52, -0.21) | 51.98 |
| Realmuto et al.2015 | -0.44 (-1.07, 0.18) | 5.59  |
| Subtotal (I-squared = 16.2%, p = 0.311) | -0.42 (-0.58, -0.27) | 100.00 |

| Hedges g (95% CI) | Weight % |
|-------------------|----------|
| Giorgi et al.2016 | -0.47 (-1.08, 0.15) | 21.65 |
| Gursoy et al.2021 | -0.64 (-1.17, -0.11) | 25.35 |
| Morou et al.2018  | 0.09 (-0.32, 0.49)  | 31.89 |
| Realmuto et al.2015 | -0.58 (-1.21, 0.05) | 21.11 |
| Subtotal (I-squared = 51.1%, p = 0.105) | -0.36 (-0.74, 0.02) | 100.00 |

| Hedges g (95% CI) | Weight % |
|-------------------|----------|
| Giorgi et al.2016 | -0.93 (-1.38, -0.48) | 21.33 |
| Gursoy et al.2021 | -0.48 (-1.00, 0.05)  | 17.79 |
| Jasionis et al.2021 | -0.45 (-0.82, -0.08) | 26.85 |
| Morou et al.2018  | -0.28 (-0.56, -0.00) | 34.03 |
| Subtotal (I-squared = 48.0%, p = 0.124) | -0.50 (-0.77, -0.23) | 100.00 |

| Hedges g (95% CI) | Weight % |
|-------------------|----------|
| Giorgi et al.2016 | -0.47 (-1.08, 0.15) | 21.23 |
| Gursoy et al.2021 | -0.64 (-1.17, -0.11) | 25.24 |
| Morou et al.2018  | 0.09 (-0.32, 0.49)  | 32.65 |
| Realmuto et al.2015 | -0.44 (-1.07, 0.18) | 20.88 |
| Subtotal (I-squared = 46.1%, p = 0.135) | -0.33 (-0.69, 0.04) | 100.00 |

| Hedges g (95% CI) | Weight % |
|-------------------|----------|
| Realmuto et al.2015 | -0.24 (-0.86, 0.38) | 100.00 |
| Subtotal (I-squared = , p = ) | -0.24 (-0.86, 0.38) | 100.00 |

Overall (I-squared = 29.9%, p = 0.113) | -0.40 (-0.52, -0.28) . |

NOTE: Weights are from random effects analysis

FIGURE 5 | Forest plots showing effect size estimates (Hedges g) for overall ToM, overall empathy, cognitive ToM, affective ToM/cognitive empathy, and affective empathy differences between IGE and healthy controls. CI, confidence interval; IGE, idiopathic generalized epilepsy; ToM, theory of mind.
# DISCUSSION

To the best of our knowledge, this meta-analysis is the first to investigate the patterns of ToM and empathy function in adult patients with epilepsy. The meta-analysis included 28 studies, and combined samples of 902 adult patients with TLE (21 studies), 205 adult patients with FLE (6 studies), 128 adult patients with IGE (5 studies), and 70 adult patients with extra-TLE/FLE (3 studies). Adult patients with TLE and FLE exhibited impairments in overall ToM, overall empathy, cognitive ToM, and affective ToM/cognitive empathy, but no significant differences were observed for affective empathy, compared to the HCs. Overall and cognitive ToM were both impaired in adult patients with IGE and extra-TLE/FLE, but no group differences were evident for overall empathy or affective ToM/cognitive empathy, compared to the HCs. Moreover, relative to the HCs, no group differences

## Table 6: Mean effects for ToM and empathy subcomponents comparing participants with Extra-TLE/FLE against HCs and tests for publication bias.

| Subcomponent   | K | N in Extra-TLE/FLE groups | N in HCs groups | g | 95% CI | Test for Heterogeneity | Assess risk of publication bias |
|----------------|---|---------------------------|-----------------|---|--------|------------------------|-------------------------------|
|                |   |                          |                 |   | Lower  | Upper  | I² statistic, % | Egger’s test P-value | Trim and fill imputed g |
| Overall ToM    | 3 | 70                        | 71              | −0.48 | −0.85  | −0.12  | 48               | 0.124 | No change |
| Overall empathy| 1 | 14                        | 29              | −0.26 | −0.71  | 0.18   | 0                | 0.342 | No change |
| CogToM         | 3 | 70                        | 71              | −0.499 | −0.88  | −0.12  | 44               | 0.342 | No change |
| AffToM/CogEmp  | 1 | 14                        | 29              | −0.26 | −0.71  | 0.18   | 0                | 0.342 | No change |

*Extra-TLE/FLE: focal seizures (caused by epileptogenic foci) outside the temporal and frontal lobes; ToM: theory of mind; CI: confidence interval; CogToM: cognitive ToM; AffToM/CogEmp: affective ToM/cognitive empathy; AffEmp: affective empathy; g: Hedges g; K: the number of studies; N: the number. Trim and fill: look for missing studies to left of mean; using random effects model. Imputed mean is random effects.*

![Forest plots showing effect size estimates (Hedges g) for overall ToM, overall empathy, cognitive ToM, and affective ToM/cognitive empathy differences between Extra-TLE/FLE and healthy controls. CI confidence interval, Extra-TLE/FLE focal seizures (caused by epileptogenic foci) outside the temporal and frontal lobes, ToM theory of mind.](image-url)
were identified for affective empathy in adult patients with IGE. The subgroup analysis found no statistically significant difference in the degree of ToM/empathy impairment between adult patients with TLE-TL- and TLE-TL+. The meta-regression analysis indicated that there was no significant relationship between the variables (age, sex, education level, age at epilepsy onset, disease duration, and monthly seizure frequency) and the magnitude of the effect sizes in adult patients with TLE. The meta-regression analysis indicated that there was no significant relationship between the variables (age, sex, education level, age at epilepsy onset, disease duration, and monthly seizure frequency) and the magnitude of the effect sizes in adult patients with TLE.

A large effect size was observed for overall ToM ($g = −0.91$, $K = 21$ and $g = −0.93$, $K = 6$) between adult patients with TLE/FLE and the HCs, which was consistent with the findings of Stewart et al. (13) ($g = −0.92$, $K = 9$ and $g = −1.03$, $K = 3$, respectively). Subsequently, we analyzed the sub-components of ToM and found that adult patients with TLE/FLE exhibited impairment in cognitive ToM ($g = −0.91$ and $g = −1.06$) and affective ToM ($g = −0.76$ and $g = −0.96$). The results may be consistent with the neuropathological progression of patients with TLE/FLE, as both the cognitive and affective ToM networks are composed of a core network, including the anterior dorsal medial prefrontal cortex and temporoparietal junction. Moreover, the cognitive ToM network involves the dorsal striatum and dorsal anterior cingulate cortex, while the affective ToM network involves the ventromedial and orbitofrontal cortices, ventral striatum, ventral anterior cingulate cortex, and amygdala (122, 123). Coincidentally, there is a clear overlap between the neural networks involved in patients with TLE/FLE and the cognitive and affective ToM networks (58, 124–132).

Moderate ($g = −0.71$, $K = 11$) and large effect sizes ($g = −0.94$, $K = 6$) were found for the comparison of overall empathy between adult patients with TLE/FLE and the HCs, respectively. Subsequently, we analyzed the sub-components of empathy and found that adult patients with TLE/FLE exhibited impairment in cognitive empathy, but no group differences were evident for affective empathy. These quantitative findings are consistent with the findings of broader research, which indicates that cognitive empathy and affective empathy are separate domains that differ in their requirements for effortful processing (27, 48, 133–135). Specifically, cognitive empathy is a slow and laborious process that requires the individual’s attention and time, while affective empathy is an automatic and spontaneous response that operates at a minimal level of consciousness (48, 136). Thus, these two components of empathy may pose different challenges for adult patients with TLE/FLE. Since the cognitive requirements for affective empathy are low, it could be expected that this ability remains relatively conserved in adult patients with TLE/FLE. Moreover, considering the limited number of included studies that contributed to the effect size of affective empathy in adult patients with TLE/FLE ($K = 3$ and $K = 1$), respectively), the findings should be interpreted with caution.

Group differences were not observed for overall empathy in adult patients with IGE and the effect size for overall ToM impairment was small ($g = −0.42$, $K = 5$), which differed from the findings of Stewart et al. (13), who conducted a meta-analysis of two studies and reported moderate impairment in the overall ToM ($g = −0.59$) in patients with IGE compared to the HCs. The results of our quantitative analyses indicated that the deficits in ToM among adult patients with IGE were subtle. This may be related to the structural abnormalities in areas recognized as ToM hubs, including the temporoparietal neocortices and medial prefrontal (137–141). Our study also focused on the sub-components of ToM. The results of previous qualitative studies suggested that the cognitive and affective ToM domains are impaired in patients with IGE (119, 141). However, these findings are inconsistent with those of the current quantitative meta-analysis, which showed that adult patients with IGE had mild impairments in cognitive ToM, but no difference was found in affective ToM. Nevertheless, these findings should be interpreted
with caution, considering the paucity of studies contributing to the effect size of affective ToM in adult patients with IGE (K = 4).

Currently, anterior temporal lobectomy (ALT) is the most common type of epilepsy surgery for adults with TLE. ALT typically entails resection of the anterior parts of temporal lobe (including the hippocampus, amygdala, anterior part of the fusiform gyrus, and adjacent neocortical temporal tissue) (114, 142), which are usually activated in ToM or empathy tasks (143). Thus, it could be hypothesized that ALT may result in the risk of a decline in ToM or empathy in patients with TLE (114, 142). However, the current quantitative findings showed no significant differences in the degree of ToM/empathy impairment between adult patients with TLE-TL- and TLE-TL+. This may be because this type of surgical treatment is commonly performed only in patients with drug resistant epilepsy; thus, most of patients with TLE-TL+ have experienced symptoms of epilepsy for many years. Such prolonged and uncontrolled seizures may cause alterations in brain tissue of epileptic zone and consequently its functions (11, 114). In addition, some of patients with TLE-TL+ suffer from epilepsy since birth or early childhood, and early-onset epilepsy may also trigger early brain reorganization, resulting in a functional compensation after surgical treatment (106). Therefore, temporal lobectomy may not significantly worsen patient’s performance in ToM or empathy tasks. However, any individual improvements or decline may be masked by group comparisons, and the results should consider methodological heterogeneity among studies (144).

LIMITATIONS

This meta-analysis had several limitations. First, we only included cross-sectional studies, while more longitudinal studies are required to investigate the dynamic changes in the ToM and empathy functions in adult patients with epilepsy. Second, although 28 studies were included in this meta-analysis, few studies contributed to the mean effect size for affective empathy between adult patients with TLE or FLE or IGE, and HCs (K = 3, K = 1, and K = 1, respectively). Additionally, only three studies provided data on the comparison between adult patients with IGE and HCs; therefore, further research in this area is warranted in the future. Third, although we investigated some demographic and clinical variables (i.e., age, sex, education level, age at epilepsy onset, disease duration, and monthly seizure frequency) that may affect ToM and empathy in adults with TLE, other factors (such as number of AEDs and IQ score) were not examined, owing to the paucity of data available in the original studies. Similarly, potential variables associated with the severity of ToM or empathy were not examined in adult patients with FLE, IGE, or extra-TLE/FLE. Further studies are needed to fully clarify the potential effects of these factors on ToM- and empathy-associated features in adult patients with epilepsy.

CONCLUSION

In conclusion, our data provide important clarifications on how the two interrelated social cognitive abilities, ToM and empathy, are affected in adults with epilepsy. The results of this meta-analysis suggest that adult patients with TLE and FLE showed impairments in cognitive ToM and affective ToM/cognitive empathy, but no significant differences were found in affective empathy. Besides, cognitive ToM was impaired in adult patients with IGE and extra-TLE/FLE, but no group differences were evident for affective ToM/cognitive empathy. Moreover, relative to the HCs, no group differences were identified for affective empathy in adult patients with IGE. Additionally, the degree of ToM/empathy impairment did not differ significantly between adult patients with TLE-TL- and TLE-TL+. These quantitative results suggest a differential impairment in the core aspects of social cognitive processing (including ToM and empathy) in adult patients with epilepsy, which may contribute to the development of structured cognitive interventions (i.e., social cognitive training) for this patient population.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

ZY and GW: study design and critical revision of the manuscript. HW, PZ, JZha, and PP: analysis and interpretation of data. HW and PZ: drafting of the manuscript. All authors approval of the final version for submission.

FUNDING

This work was supported by the Jiangsu Commission of Health (LYG20180390).

ACKNOWLEDGMENTS

We thank all authors of the studies included. This protocol was prospectively registered at the International Platform of Registered Systematic Review and Meta-analysis Protocols (ID: INPLASY2021120039).

REFERENCES

1. Thijs RD, Surges R, O’Brien TJ, Sander JW. Epilepsy in adults. Lancet. (2019) 393:689–701. doi: 10.1016/s0140-673632596-0

2. Adamczyk B, Węgrzyn K, Wilczyński T, Maciarz J, Morawiec N, Adamczyk-Sowa M. The most common lesions detected by neuroimaging as causes of epilepsy. Medicina (Kaunas). (2021) 57:294. doi: 10.3390/medicina57030294
3. GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol*. (2019) 18:459–80. doi: 10.1016/s1474-4423(19)30499-x

4. Janson MT, Bainbridge JL. Continuing burden of refractory epilepsy. *Ann Pharmacother*. (2021) 55:406–8. doi: 10.1177/1060022820948056

5. Tombini M, Assenza G, Quintiliani L, Ricci L, Lanzone J, Dl Lazzaro V. Epilepsy and quality of life: what does really matter? *Neuroulon Sci*. (2021) 42:3757–65. doi: 10.1016/j.clinph.2020.09.006

6. Martin RC, Griffith HR, Faught E, Gilman F, Mackey M, Vogtle L. Cognitive functioning in community dwelling older adults with chronic partial epilepsy. *Epilepsia*. (2005) 46:298–303. doi: 10.1111/j.1365-2913.2005.01044.x

7. Griffith HR, Martin RC, Barbara JK, Marson DC, Faught E. Older adults with epilepsy demonstrate cognitive impairments compared with patients with amnestic mild cognitive impairment. *Epilepsy Behav*. (2006) 8:161–8. doi: 10.1016/j.yebeh.2005.09.003

8. Piazzini A, Canevini MP, Turner K, Chifari R, Canger R. Elderly people and epilepsy: cognitive function. *Epilepsia*. (2006) 47(Suppl. 5):82–4. doi: 10.1111/j.1528-1167.2006.00884.x

9. Griffith HR, Martin RC, Barabra JK, Faught E, Vogtle LK, Marson DC. Cognitive functioning over 3 years in community dwelling older adults with chronic partial epilepsy. *Epilepsy Res*. (2007) 74:91–6. doi: 10.1016/j.yeber.2007.01.002

10. Witti JA, Werhahn KJ, Krammer G, Ruches C, Trinka E, Helmstaedter C. Cognitive-behavioral screening in elderly patients with new-onset epilepsy before treatment. *Acta Neurol Scand*. (2014) 130:172–7. doi: 10.1111/ane.12260

11. Bora E, Meletti S. Social cognition in temporal lobe epilepsy: a systematic review and meta-analysis. *Epilepsia*. (2016) 56:401–7. doi: 10.1111/epi.13597

12. Miller LA, Galioto R, Tremont G, Davis J, Bryant K, Roth J, et al. Cognitive impairment in older adults with epilepsy: characterization and risk factor analysis. *Epilepsy Behav*. (2016) 56:113–7. doi: 10.1016/j.yebeh.2016.01.011

13. Stewart E, Catroppa C, Lah S. Theory of mind in patients with epilepsy: a systematic review and meta-analysis. *Neurosc Phylosoc*. (2016) 26:3–24. doi: 10.1016/j.tics.2016.01.011

14. Sen A, Capelli V, Huisan M. Cognition and dementia in older patients with epilepsy. *Brain*. (2018) 141:1592–608. doi: 10.1093/brain/awy022

15. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association (2013).

16. Baron-Cohen S. Is asperger syndrome/high-functioning autism necessarily a disability? *Dev Psychopathol*. (2000) 12:489–500. doi: 10.1017/s135560030001326

17. Brune M, Brune-Coehrs U. Theory of mind—evolution, ontogeny, brain mechanisms and psychopathology. *Neuroul Biobehav Rev*. (2006) 30:437–55. doi: 10.1016/j.neubiorev.2005.08.001

18. Call J, Tomasetto M. Does the chimpanzee have a theory of mind? 30 years later. *Trends Cog Sci*. (2008) 12:187–92. doi: 10.1016/j.tics.2008.02.010

19. Henry A, Tourbah A, Chauin MP, Rumbach L, Montreuil M, Bakhine S. Social cognition impairments in relapsing-remitting multiple sclerosis. *J Int Neuropsychol Soc*. (2011) 17:1122–31. doi: 10.1017/s1355617711001147

20. Lin X, Zhang X, Liu Q, Zhao P, Zhang H, Wang H, et al. Theory of mind in adults with traumatic brain injury: a meta-analysis. *Neurosci Biobehav Rev*. (2021) 121:106–18. doi: 10.1016/j.neubiorev.2020.12.010

21. McDonald S, Flanagan S. Social perception deficits after traumatic brain injury: interaction between emotion recognition, mentalizing ability, and social communication. *Neropsychology*. (2004) 18:572–9. doi: 10.1037/0894-4105.18.3.572
47. Coundoursis SP, Adams AG, Henry JD. Empathy and theory of mind in Parkinson’s disease: a meta-analysis. Neurosci Biobehav Rev. (2020) 109:92–102. doi: 10.1016/j.neubiorev.2019.12.030

48. Demichels OP, Coundoursis SP, Grainger SA, Henry JD. Empathy and theory of mind in Alzheimer’s disease: a meta-analysis. Int J Neuropsychol Soc. (2020) 26:963–77. doi: 10.1016/j.ijsns.2020.04.016

49. Shaw DJ, Czekóňová K, Pennington CR, Qureshi AW, Špilaková B, Salazar M, et al. You ≠ me: individual differences in the structure of social cognition. Psychol Rev. (2020) 84:1139–56. doi: 10.1037/0042-0185-11-107-3

50. Schurz M, Radua J, Tholen MG, Maliske L, Margulies DS, Mars RB, et al. Toward a hierarchical model of social cognition: a neuroimaging meta-analysis and integrative review of empathy and theory of mind. Psychol Bull. (2021) 147:293–327. doi: 10.1037/bul0000030

51. Jiang Y, Hu Y, Wang Y, Zhou N, Zhu L, Wang K. Empathy and emotion recognition in patients with idiopathic generalized epilepsy. Epilepsy Behav. (2014) 37:139–44. doi: 10.1016/j.yebeh.2014.06.005

52. Hennion S, Szurhaj W, Duhamel A, Lopes R, Tyvaert L, Derambure P, et al. Characterization and prediction of the recognition of emotional faces and emotional bursts in temporal lobe epilepsy. J Clin Exp Neurophysiol. (2015) 37:931–45. doi: 10.1080/13803395.2015.1068280

53. Hu Y, Jiang Y, Hu P, Ma H, Wang K. Impaired social cognition in patients with interictal epileptiform discharges in the frontal lobe. Epilepsy Behav. (2016) 57:36–54. doi: 10.1016/j.yebeh.2016.01.027

54. Gul A, Ahmad H. The relationship between dispositional empathy and frontal cortical functioning in patients with frontal lobe epilepsy. Pak J Med Sci. (2017) 33:200–4. doi: 10.12669/pjms.33.11742

55. Jiang Y, Zhu M, Yu F, Wang K. Impaired empathy in patients with idiopathic generalized epilepsy: an event-related potentials study. Epilepsy Behav. (2020) 111:107274. doi: 10.1016/j.yebeh.2020.107274

56. Shaw P, Lawrence E, Bramham J, Brieler B, Radbourne C, David AS. A prospective study of the effects of anterior temporal lobectomy on emotion recognition and theory of mind. Neuropsychologia. (2007) 45:2783–90. doi: 10.1016/j.neuropsychologia.2007.04.020

57. Boucher O, Rouleau I, Lassonde M, Lepore F, Bouthillier A, Nguyen DK. Social information processing following resection of the insular cortex. Neuropsychologia. (2015) 71:1–10. doi: 10.1016/j.neuropsychologia.2015.03.008

58. Hennion S, Delbeuck X, Koelkebeck K, Brion M, Tyvaert L, Plomhause P, et al. A functional magnetic resonance imaging investigation of theory of mind impairments in patients with temporal lobe epilepsy. Neuropsychologia. (2016) 93:271–9. doi: 10.1016/j.neuropsychologia.2016.11.007

59. Braams OB, Meekes J, van Nieuwenhuizen O, Schappin R, van Rijen PC, Blijd-Hoogewys EMA, et al. Epilepsy surgery in children: no further threat in the long-term. Eur J Paediatr Neurol. (2020) 28:167–75. doi: 10.1016/j.ejpn.2020.06.019

60. Lomolodijan C, Múnera CP, Low DM, Terpiluk V, Solis P, Abusamra V, et al. The right hemisphere’s contribution to discourse processing: a study in temporal lobe epilepsy. Brain Lang. (2017) 171:31–41. doi: 10.1016/j.bandl.2017.04.001

61. Sung C, Connor A. Social-cognitive predictors of vocational outcomes in transition youth with epilepsy: application of social cognitive career theory. Rehabil Psychol. (2017) 62:276–89. doi: 10.1037/rep0000161

62. Abraira L, Sanabria A, Ortega G, Quintana M, Santamarina E, Salas-Puig J, et al. [Social cognition and cognitive functions in patients with epilepsy treated with eslicarbazepine acetate]. Rev Neurol. (2018) 66:361–7.

63. Inanç L, Ünal Y, Semiz ÜB, Kulu F. Do mentalization skills affect the perception of stigma in patients with epilepsy? Epilepsy Behav. (2018) 88:49–53. doi: 10.1016/j.yebeh.2018.08.022

64. Grewe P, Schulz R, Woermann FG, Brandt C, Doll A, Hoppe M, et al. Very long-term outcome in resected and non-resected patients with temporal lobe epilepsy with medial temporal lobe sclerosis: a multiple case-study. Seizure. (2019) 67:30–7. doi: 10.1016/j.seizure.2019.02.015

65. Giovagnoli AR, Canafoglia L, Reati F, Raviglione F, Franceschetti S. The neuropsychological pattern of Uvnerricht-Lundborg disease. Epilepsy Res. (2009) 84:217–23. doi: 10.1016/j.eplepsyres.2009.02.004

66. Toller G, Adhimoolam B, Gruenwald T, Huppertz HJ, Kurthen M, Rankin KP, et al. Right mesial temporal lobe epilepsy impairs empathy-related brain responses to dynamic fearful faces. J Neurol. (2015) 262:729–41. doi: 10.1007/s00415-014-7622-2

67. Kuchukhidze G, Höfler J, Kronbichler M, Schmid E, Kirschnier M, L, et al. Emotion recognition and social cognition in juvenile myoclonic epilepsy. Z Epileptol. (2019) 32:177–82. doi: 10.1016/s1030-0919-0261-y

68. Lunn J, Lewis C, Gannon E. Parent-child mentalizing in pediatric epilepsy. Epilepsy Behav. (2019) 96:6–12. doi: 10.1016/j.yebeh.2019.03.052

69. Shiota MN, Simpson ML, Kirsch HE, Levenson RW. Emotion recognition in objects in patients with neurological disease. Neuropsychologia. (2019) 133:1163–73. doi: 10.1016/j.neuropsychologia.2018.09.015

70. Operto FF, Pastorino GMG, Padovano C, Scuoppo C, Vivenzio V, Coppola G. Social cognition in neuropsychiatric disorders in pediatric age. Brain. (2020) 11:81–8. doi: 10.18662/brain/11.3sup1/124

71. Genizi J, Shamay-Tsoory SG, Sharaer E, Yaniv S, Aharon-Perez J. Impaired social behavior in children with benign childhood epilepsy with centrotemporal spikes. J Child Neurol. (2012) 27:156–61. doi: 10.1177/0883073811441420

72. Lew AR, Lewis C, Lunn J, Tomlin P, Basu H, Roach J, et al. Social cognition in children with epilepsy in mainstream education. Dev Med Child Neurol. (2015) 57:53–9. doi: 10.1111/dmcn.12613

73. Lunn J, Lewis C, Sherlock C. Impaired performance on advanced theory of Mind tasks in children with epilepsy is related to poor communication
and increased attention problems. *Epilepsy Behav.* (2015) 43:109–16. doi: 10.1016/j.yebeh.2014.11.010

89. Raul T, Kaldoja ML, Kolk A. Relationship between social competence and neurocognitive performance in children with epilepsy. *Epilepsy Behav.* (2015) 52:93–101. doi: 10.1016/j.yebeh.2015.08.018

90. Zali T, Zanini S, Conte S, Borgetti R, Urgesi C. Neuropsychological assessment of children with epilepsy and average intelligence using NEPSY II. *J Clin Exp Neuropsychol.* (2015) 37:1036–51. doi: 10.1080/13803955.2015.1076380

91. Stewart E, Catroppa C, Gill D, Webster R, Lawson J, Mandalis A, et al. Theory of mind and social competence in children and adolescents with genetic generalised epilepsy (GGE): relationships to epilepsy severity and anti-epileptic drugs. *Seizure.* (2018) 60:96–104. doi: 10.1016/j.seizure.2018.06.015

92. Zhang T, Chen L, Wang Y, Zhang M, Wang L, Xu X, et al. Impaired theory of mind in Chinese children and adolescents with idiopathic generalised epilepsy: association with behavioral manifestations of executive dysfunction. *Epilepsy Behav.* (2018) 79:205–12. doi: 10.1016/j.yebeh.2017.12.006

93. Stewart E, Catroppa C, Gonzalez L, Gill D, Webster R, Lawson J, et al. Theory of mind and social competence in children and adolescents with temporal lobe epilepsy. *Neuropsychology.* (2019) 33:986–95. doi: 10.1037/neu0000543

94. Bailey K, Im-Bolter N. Theory of mind and language in childhood epilepsy. *Mind Brain Educ.* (2010) 4:14–64. doi: 10.1111/mbe.12230

95. Lima EM, Rzezak P, Montenegro MA, Guerreiro MM, Valente KDR. Social cognition in childhood epilepsy with centrotemporal spikes. *Seizure.* (2020) 78:102–8. doi: 10.1016/j.seizure.2020.03.014

96. Pastorino GM, Operto FF, Padovano C, Vivenzio V, Scaoppo C, Pastorino N, et al. Social cognition in neurodevelopmental disorders and epilepsy. *Front Neurol.* (2012) 2:658823. doi: 10.3389/fneur.2012.0658823

97. Wu L, Yang X, Zhang K, Wang X, Yang B. Impairment of eye emotion discrimination in benign childhood epilepsy with centrotemporal spikes: a neuropsychological study. *Brain Behav.* (2011) 11:e02154. doi: 10.1002/brb3.2154

98. Shaw P, Lawrence EI, Radbourne C, Bramham J, Polkey CE, David AS. The effect of epilepsy surgery. *Epilepsia.* (2015) 56:1117–23. doi: 10.1111/epi.13384

99. Wang WH, Shih YH, Yu HY, Jen DJ, Lin YY, Kwan SY, et al. Theory of mind and social functioning in patients with temporal lobe epilepsy. *Epilepsia.* (2015) 56:1117–23. doi: 10.1111/epi.13384

100. Zhang T, Chen L, Wang Y, Zhang M, Wang L, Xu X, et al. Impaired theory of mind in patients with epilepsy: evidence from patients with temporal lobe and idiopathic generalized epilepsies. *Epilepsy Behav.* (2015) 47:98–103. doi: 10.1016/j.yebeh.2015.04.048

101. Giovagnoli AR, Parente A, Didato G, Deleo F, Villani F. Expanding the spectrum of cognitive outcomes after temporal lobe epilepsy surgery: a prospective study of theory of mind. *Epilepsia.* (2016) 57:920–30. doi: 10.1111/epi.13384

102. Giovagnoli AR, Parente A, Didato G, Deleo F, Villani F. Expanding the spectrum of cognitive outcomes after temporal lobe epilepsy surgery: a prospective study of theory of mind. *Epilepsia.* (2016) 57:920–30. doi: 10.1111/epi.13384

103. Giovagnoli AR, Bala A, Dziekan M, Szantroch M, Rysz A, Marchel A, et al. Gaze matters! The effect of gaze direction on emotional enhancement of memory for faces in patients with mesial temporal lobe epilepsy. *Epilepsy Behav.* (2017) 72:35–8. doi: 10.1016/j.yebeh.2017.04.016

104. Giovagnoli AR, Bala A, Wordecha M, Jarikiewicz M, Wysokinska E, Szczepcowa E, et al. Social cognition in neuropsychiatric populations: a comparison of theory of mind in schizophrenia and mesial temporal lobe epilepsy. *Sci Rep.* (2017) 7:484. doi: 10.1038/s41598-017-00565-2

105. Amlerova J, Cavanna AE, Bradac O, Javurkova A, Raudenska J, Marusic M, et al. Social cognition in temporal lobe epilepsy and lobectomy: risk factors and neural substrates. *Epilepsia.* (2013) 54:1995–2002. doi: 10.1111/j.1528-1167.2012.03255.x

106. Bortolotti SD, Kuchukhidze G, Grunwald T, Kraemer G, Kurthen M, Jokeit H. “Tell me how do I feel”—emotion recognition and theory of mind in symptomatic mesial temporal lobe epilepsy. *Neuropsychologia.* (2012) 50:118–28. doi: 10.1016/j.neuropsychologia.2011.11.005

107. Giovagnoli AR, Parente A, Villani F, Franceschetti S, Sprefaci R. Theory of mind and epilepsy: what clinical implications? *Epilepsia.* (2013) 54:1639–46. doi: 10.1111/epi.12255

108. Cohn M, St-Laurent M, Barnett A, MacAndrews MP. Social inference deficits in temporal lobe epilepsy and lobectomy: risk factors and neural substrates. *Soc Cogn Affect Neurosci.* (2015) 10:636–44. doi: 10.1093/scan/nau101

109. Hennon S, Delbeuck X, Duhamel A, Lopes R, Semah F, Tysvaert L, et al. Characterization and prediction of theory of mind disorders in temporal lobe epilepsy. *Neuropsychology.* (2015) 29:485–92. doi: 10.1037/neu0000126

110. Realmutu S, Zummo L, Cerami C, Agro L, Dodich A, Canessa N, et al. Social cognition dysfunctions in patients with epilepsy: evidence from patients with
disease/mild cognitive impairment: a review. *Neuroradiology*. (2010) 52:711–
21. doi: 10.1007/s00234-010-0717-2

129. Liao W, Zhang Z, Pan Z, Mantini D, Ding J, Duan X, et al. Altered functional
connectivity and small-world in mesial temporal lobe epilepsy. *PLoS One*. (2010) 5:e8525. doi: 10.1371/journal.pone.0008525

130. Broicher SD, Frings L, Huppertz HJ, Grunwald T, Kurthen M, Krämer G, et al. Alterations in functional connectivity of the amygdala in unilateral mesial temporal lobe epilepsy. *J Neurol*. (2012) 259:2546–54. doi: 10.1007/s00415-012-6533-3

131. Ives-Deliperi VL, Jokeit H. Impaired social cognition in epilepsy: a review of what we have learnt from neuroimaging studies. *Front Neurol*. (2019) 10:940. doi: 10.3389/fneur.2019.00940

132. Broicher SD, Frings L, Huppertz HJ, Grunwald T, Kurthen M, Krämer G, et al. Alterations in functional connectivity of the amygdala in unilateral mesial temporal lobe epilepsy. *J Neurol*. (2012) 259:2546–54. doi: 10.1007/s00415-012-6533-3

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Wang, Zhao, Zhao, Pan, Wang and Yi. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.