The aim of this study is to conduct a meta-analysis to characterize theory of mind and empathy performance in adults with epilepsy.

**Condition being studied:**
Epilepsy is one of the most common neurological disorders, affecting over 50 million people worldwide. Cognitive impairment is considered a common symptom of epilepsy, including memory impairment, language dysfunction, attention deficit, executive dysfunction, and social cognition impairment. Social cognition is defined as the ability to explain and predict the behavior of others based on the beliefs, feelings, and intentions of others, and to interact in complex social environments and relationships. Social cognition is a multidimensional construct, mainly involving: theory of mind (ToM), empathy, social perception, and social knowledge, and attribution bias. However, there have been inconsistent findings. However, no previous meta-analysis has investigated the difference between cognitive ToM and affective ToM in adult patients with epilepsy, and it is not clear how empathy abilities are affected in adult patients with epilepsy.

**INPLASY registration number:**
This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 December 2021 and was last updated on 07 December 2021 (registration number INPLASY2021120039).
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METHODS

Search strategy: A systematic literature search was conducted across the PubMed, Web of Science, and Embase databases from inception to November 20th, 2021. The following search terms were used: “epileps*” or “seizure disorder” combined with: “social cognition” or “theory of mind” or “ToM” or “mentalizing” or “empath*” or “perspective taking”. Furthermore, other resources, such as the reference lists of all included studies, were searched manually.

Participant or population: Adult patients with epilepsy. No restrictions on sex, ethnicity, education or economic status.

Intervention: Studies compare ToM and empathy performance between a group of adult patients with epilepsy and a sample of healthy controls.

Comparator: ToM and empathy performance.

Study designs to be included: Case-control studies.

Eligibility criteria: Studies were included if they met the following five criteria: 1) the study was published as in English a primary peer-reviewed research article; 2) the study assessed at least one domain of ToM or empathy performance using standard measures; 3) the study compared ToM or empathy performance between the patients with epilepsy and HCs; 4) the study provided sufficient data to calculate effect sizes of ToM or empathy. 5) the study had to include individuals with epilepsy ≥18 years. Studies were excluded, to ensure the reliability of the outcome for the following reasons: 1) the study lacked comparisons of ToM or empathy between patients with epilepsy and HCs; 2) the sample overlapped with another study with larger sample size; 3) studies that grouped patients with different site of seizure focus together; and 4) the sample size was less than 10.

Information sources: Electronic databases (including PubMed, Web of Science, and Embase) have to be searched from inception to November 20th, 2021. There were no restrictions of the age of patients or phenotype of epilepsy for inclusion. In addition, other resources will be searched manually, such as the references of all included studies.

Main outcome(s): Primary outcomes will include ToM and empathy tasks used. Besides, the data used for calculating the effect sizes and standard errors of the ToM/ empathy tasks will be included.

Additional outcome(s): Additional outcomes will include the questionnaire of clinical symptoms of epilepsy.

Quality assessment / Risk of bias analysis: We will use the Newcastle-Ottawa Quality Assessment Scale (NOS) to assess the quality of all included studies.

Strategy of data synthesis: Stata 15.0 software will be used for data analysis and quantitative data synthesis. The effect size (Hedges g) and 95% confidence interval (CI) will be calculated to estimate differences in ToM and empathy between
the patients with epilepsy and HCs. For studies reporting more than one ToM task, pooled effect sizes and standard error value will be calculated. Similarly, the empathy performance will be calculated.

**Subgroup analysis:** To provide the first meta-analytic integration of ToM and empathy in adult patients with epilepsy, and to investigate the cognitive and affective subcomponents of these two abilities, subgroup analysis will be performed in different components (cognitive ToM, affective ToM/cognitive empathy, and affective empathy), and epilepsy subtypes (such as TLE, FLE, extra-TLE/FLE, and IGE).

**Sensitivity analysis:** We will conduct a sensitivity analysis to test the influence of each dataset, methodological quality, and the potential impacts of missing data on the pooled results. If publication bias was found, we will apply the trim-and-fill method to provide effect sizes adjusted for publication bias.

**Language:** English.

**Country(ies) involved:** China.

**Keywords:** epilepsy, theory of mind, empathy, meta-analysis.

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