Theory of Mind and Its Brain Distribution in Patients with Temporal Lobe Epilepsy

Wei-Han Wang, Hsiang-Yu Yu, Mau-Sun Hua

Abstract—Theory of Mind (ToM) refers to the ability to infer another's mental state. With appropriate ToM, one can behave well in social interactions. A growing body of evidence has demonstrated that patients with temporal lobe epilepsy (TLE) may damage ToM by affecting on regions of the underlying neural network of ToM. However, the question of whether there is cerebral laterality for ToM functions remains open. This study aimed to examine whether there is cerebral lateralization for ToM abilities in TLE patients. Sixty-seven adult TLE patients and 30 matched healthy controls (HC) were recruited. Patients were classified into right (RTLE), left (LTLE), and bilateral (BTLE) TLE groups on the basis of a consensus panel review of their seizure semiology, EEG findings, and brain imaging results. All participants completed an intellectual test and four tasks measuring basic and advanced ToM. The results showed that, on all ToM tasks, (1) each patient group performed worse than HC; (2) there were no significant differences between LTLE and RTLE groups; and (3) the BTLE group performed the worst. It appears that the neural network responsible for ToM is distributed evenly between the cerebral hemispheres.

Keywords—Cerebral lateralization, social cognition, temporal lobe epilepsy, theory of mind.

I. INTRODUCTION

EPILEPSY is a chronic disorder characterized by recurrent seizures and has significant cognitive and psychosocial consequences for everyday living [1], [2]. People with epilepsy (PWE), even those with well-controlled seizures, may face poor interpersonal relationships, reduced social interactions, decreased job opportunities, and problems in daily activities. The relationship between social cognition and psychosocial function in PWE has been gaining considerable attention in recent years. The influence of social cognition on psychosocial function in people with epilepsy has been gaining considerable attention in recent years. Social cognition refers to how people perceive and interpret social information, and how well they respond to this information [3], [4] A key aspect of social cognition is the ability to conceptualize other people's thoughts, intentions, and desires; this is known as "theory of mind" (ToM) [3], [4]. Numerous studies suggest that multiple brain regions—mainly the medial prefrontal cortices, superior temporal sulcus, temporoparietal junction, bilateral temporal poles, and amygdala—might be associated with ToM

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functioning. [5]-[9]

Temporal lobe epilepsy (TLE), a common type of focal epilepsy, is characterized by epileptogenic discharges arising from temporal regions. A growing body of evidence has demonstrated that TLE may damage ToM by impacting on regions of the underlying neural network of ToM.3, [10]-[15]. Nevertheless, the question of whether there is cerebral laterality for ToM functions remains open. Schacher et al. [12] found that their patients with right TLE performed worse than those with left TLE on the ToM (Faux Pas Recognition) task. However, such findings conflict with the observations of two other studies [13], [14]. Methodological differences might account for such contradictory results. For instance, most previous studies focused merely on specific aspects of advanced, rather than on both primary and advanced ToM in their patients.

In view of the above reason, we employed an intellectual test and four standardized ToM tasks (measuring basic and advanced ToM) to examine whether there is a cerebral laterality for ToM abilities in TLE patients.

II. METHODS

A. Subjects

This study was approved by the institutional ethics committee of the Taipei Veterans General Hospital (TPEVGH), one of the largest medical centers in Taiwan. At enrollment, written informed consent was obtained from all participants. Sixty-seven adult inpatients with TLE were recruited from the Neurological Institute at TPEVGH. All patients were diagnosed with medically refractory epilepsy by experienced epileptologists, according to the criteria defined by the International League Against Epilepsy. None of the patients had undergone brain surgery before recruitment. Patients were classified into right (RTLE; n = 24), left (LTLE; n = 28), and bilateral (BTLE; n = 15) TLE groups on the basis of a consensus panel review of their seizure semiology, EEG findings, and brain imaging results. Moreover, Thirty healthy controls (HC) were selected and underwent all tests. Participants with abnormal MRI findings outside the temporal regions and a history (or current diagnosis) of neurodevelopmental disorders (such as autism spectrum disorder and attention deficit hyperactivity disorder), neurodegenerative diseases, major depression, anxiety disorders (including social phobia), mental retardation, physical limitations, and severe systemic disease were excluded.

B. ToM Tasks

Four standardized ToM tasks in Chinese, [15] the False

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Belief (FB) test, Faux Pas Recognition (FPR) test, Implication Stories (IS) test, and Visual Cartoon (VC) test, were used to measure ToM ability. The internal consistency coefficients (Cronbach's α values) of the tasks were 0.50 for the first-order FB test, 0.67 for the second-order FB test, 0.91 for the FPR test, 0.93 for the IS test, 0.87 for the VC test in implicit form, and 0.92 for the VC test in explicit form. Moreover, based on a sample of 32 healthy adults, test-retest reliabilities for the tasks ranged from 0.86 to 0.94 [13]. Following the procedure of Li. et al.,[2] we employed the FB test to assess basic ToM, and used the FPR, IS, and VC tests to evaluate advanced ToM abilities. To minimize the load on memory, all ToM materials were presented to participants during the administration [4], [15].

The FB test comprises 8 stories, based on the paradigm used in the studies by Wimmer and Perner [16]. Each story is followed by a test question to assess whether participants can recognize that the characters have beliefs about the world that are different from their own perspectives. In addition, two control questions (e.g., "Where is the object really?" and "Where was the object in the beginning?") were used to ensure that participants had understood and remembered the contents. Participants needed to pass both control questions to qualify for scoring on each trial. For each story, 1 point is given for each correct answer with a false belief. The total score for the FB test ranges from 0 to 8.

The FPR test consists of 10 stories, all of which describe a situation where a speaker says something that is socially inappropriate [17]. Each story is followed by 3 test questions intended to evaluate whether participants recognized the inappropriateness of the speaker's remarks and realized that these remarks could have negative consequences for the listener that the speaker did not intend (a "faux pas"). A control question ensured that the participants had understood the story and were paying attention. After passing the control question, 1 point is given for each correct answer to the test questions. The total score for the FPR test ranges from 0 to 30.

The IS test comprises 5 short stories with implied meaning, such as a joke, white lie, or pretend situation [18]. Each story is followed by two questions to assess whether participants could understand the implied meaning in the story. The total score for the IS test ranges from 0 to 10.

The VC test includes 10 funny cartoon pictures. Participants are shown the pictures one at a time, with two types of questions intended to assess their abilities to infer the characters' mental states. The first question is open-ended (implicit form), asking participants why the picture is funny; the second question is presented in a more explicit manner (explicit form), asking what the motives of the character in each picture are. The total score for each type of question ranges from 0 to 20.

C. Intellectual Assessment

The Taiwanese version of the Wechsler Adult Intelligence Scale-Third edition (WAIS-III) [19] was used to evaluate intellectual function.

D. Statistical Analysis

The TLE and HC groups were compared using a t test for parametric variables and a χ^2 test for categorical variables. An analysis of variance (ANOVA) with Scheffé post hoc pairwise comparisons was performed to determine significant differences between the groups. However, if the data violated the assumption of homogeneity of variance, the Kruskal-Wallis test with Mann-Whitney pairwise comparisons was used. A multivariate analysis of covariance (MANCOVA) with Fisher's Least Significant Difference (LSD) pairwise comparisons was also used to compare performance on tests across groups if needed.

III. RESULTS

As shown in Table I, demographic variables did not differ between TLE and HC groups, with the exception of the intellectual function.

A MANCOVA with LSD test was therefore performed to parse out the contribution of intellectual function to ToM tasks. The results (Table II) showed that (1) each patient group performed worse than HC on the FB test ($F_{3,92} = 5.91$; p < 0.01), FPR test ($F_{3,92} = 6.46$; p < 0.01), IS test ($F_{3,92} = 12.02$; p < 0.01), and VC test (Implicit form: $F_{3,92} = 10.28$, p < 0.001; Explicit form: $F_{3,92} = 12.32$, p < 0.001); (2) there were no significant differences between LTLE and RTLE groups on all ToM tasks; and (3) the BTLE group performed the worst on all ToM tasks as expected (all p < 0.01).

TABLE I
CHARACTERISTICS OF THE DEMOGRAPHIC VARIABLES

	LTLE n = 28 Mean (SD)	RTLE n = 24 Mean (SD)	BTLE n = 15 Mean (SD)	HC n = 30 Mean (SD)	Statistics Value	p-value
Gender (Male/Female)	13/15	13/11	10/5	16/14	$\chi^2_1 = 0.001$ [a]	0.971
Age (years)	34.89 (11.37)	30.92 (9.56)	29.20 (8.13)	33.40 (9.57)	$F_{3,93} = 1.38$ [b]	0.254
Education (years)	13.93 (2.54)	14.13 (2.33)	12.60 (2.53)	14.33 (2.11)	$F_{3,93} = 1.93$ [b]	0.130
Intellectual Function*	93.29 (13.93) [c]	96.38 (12.69)	87.53 (8.75) [c]	102.93 (6.62)	$\chi^2_3 = 20.81$	<0.001

LTLE = left temporal lobe epilepsy; RTLE = right temporal lobe epilepsy; BTLE = bilateral temporal lobe epilepsy; HC = healthy controls. * Intellectual Function was evaluated through the Taiwanese version of the Wechsler Adult Intelligence Scale-Third edition. [a] Chi-Squre test [b] Analysis of variance with Scheffe post hoc comparison. [c] Significantly lower than HC; Kruskal-Wallis Test with Mann-Whitney pairwise comparison was used because the data violated the assumption of homogeneity of variance.

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TABLE II
PERFORMANCE ON TOM TASKS IN PATIENTS WITH TLE AND HC

	LTLE $n = 28$ Mean (SD)	RTLE $n = 24$ Mean (SD)	BTLE $n = 15$ Mean (SD)	HC $n = 30$ Mean (SD)	Statistics Value	p-value
ToM Abilities						
FB	6.32 (1.31) [a]	6.38 (1.21) [a]	5.13 (1.51) [a,b,c]	7.50 (0.73)	$F_{3,92} = 5.91$	0.001
FPR	25.07 (3.04) [a]	24.96 (2.79) [a]	21.40 (5.05) [a,b,c]	27.77 (1.33)	$F_{3,92} = 6.46$	0.001
IS	7.25 (1.51) [a]	7.21 (1.50) [a]	5.73 (2.01) [a,b,c]	9.40 (0.68)	$F_{3,92} = 12.02$	<0.001
VC_Implicit form	12.57 (2.28) [a]	12.25 (2.27) [a]	9.53 (2.99) [a,b,c]	15.23 (1.83)	$F_{3,92} = 10.28$	<0.001
VC_Explicit form	13.61 (1.97) [a]	13.21 (2.09) [a]	11.20 (2.46) [a,b,c]	16.30 (1.56)	$F_{3,92} = 12.32$	<0.001

ToM = theory of mind; TLE = temporal lobe epilepsy; HC = healthy controls; LTLE = left temporal lobe epilepsy; RTLE = right temporal lobe epilepsy; BTLE = bilateral temporal lobe epilepsy; FB = False Belief test; FPR = Faux Pas Recognition test; IS = Implication Stories test; VC = Visual Cartoon tasks. [a] Significantly lower than HC; MANCOVA with Fisher's Least Significant Difference (LSD) test was performed to parse out the contribution of intellectual function. [b] BTLE < LTLE; MANCOVA with LSD test was performed to parse out the contribution of intellectual function. [c] BTLE < RTLE; MANCOVA with LSD test was performed to parse out the contribution of intellectual function.

IV. DISCUSSION

The main goal of the current study was to investigate whether there is a cerebral laterality for ToM abilities in TLE patients. The results revealed that patients with TLE exhibited impairments in both basic and advanced ToM. Moreover, BTLE patients performed the worst on all ToM tasks, but there were no significant differences between left or right TLE patients.

In line with previous studies [4], [10]-[13], we found that patients with TLE did show impairments in ToM abilities. Unlike the previous studies,[10]-[13] we further demonstrated that patients with TLE have impairments in both basic and advanced ToM, evidenced by deficits in false belief reasoning, faux pas recognition, the ability to comprehend implied meanings in the verbal stories, and the ability to infer others' mental states via visual material.

In general, we found no differences between LTLE and RTLE groups on all ToM tasks. This is consistent with Broicher and colleagues' study, [10] in which performance on the FPR test did not significantly differ between patients with seizures originating within the left versus right mesial temporal lobe. It appears that the neural network responsible for ToM is distributed evenly between the cerebral hemispheres. In fact, a recent review, [9] which used a meta-analysis with the activation-likelihood estimation approach, indicated that the core mentalizing (i.e., ToM) neural network is larger than previously described, including the medial PFCs, bilateral posterior superior temporal sulcus, bilateral angular gyri, bilateral anterior temporal areas, posterior cingulate cortex and precuneus, and possibly the left inferior temporal gyrus. Taken together, our results indicate that patients with broader epileptogenic regions (e.g., bilateral TLE) are more likely to have ToM deficits, whereas unilateral TLE patients have limited ToM impairment. We suggest that measurement of ToM ability be included in the regular neuropsychological assessment of patients with TLE.

Finally, a number of limitations must be considered in the present study. First, considering the low internal consistency for the first-order FB test, this task might not be ideal for measuring basic ToM effectively. Second, we explored the effect of social cognitive dysfunction by examining ToM abilities. However, an increasing number of studies have indicated that, in addition to ToM abilities, both emotion and social perception play an important role in social cognition [20]. Thus, a comprehensive test encompassing these dimensions of social cognition (e.g., The Awareness of Social Inference Test [20]) is needed for future studies.

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