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Impaired social cognition in patients with interictal epileptiform discharges in the frontal lobe

Ying Hu, Yubao Jiang, Panpan Hu, Huijuan Ma, Kai Wang *

Department of Neurology, The First Affiliated Hospital of Anhui Medical University, No. 218 of JiXi Road, 230022 Hefei City, Anhui Province, PR China

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ABSTRACT

Background: Patients with epilepsy frequently experience cognitive impairments, including impairments in social cognition. However, there is a lack of direct examinations of the affective and cognitive aspects of social cognition in such patients. The neural correlates remain to be identified. The present study was designed to examine the degree of impairments in different aspects of social cognition including empathy, emotion recognition, and Theory of Mind (ToM) in patients with epilepsy. In addition, we further explored factors related to the impairments, highlighting the specific importance of the frontal region.

Materials and methods: After 24-hour EEG monitoring, 53 patients with epilepsy were administered a neuropsychological battery of tests for basic intelligence assessment and then were tested with the Interpersonal Reactive Index, the "Yoni" task, the Emotion Recognition Test, the Reading the Mind in the Eyes test, and other neuropsychological tests. The clinical variables potentially affecting the ability to accomplish these tests were taken into account. We divided the patients into those having frontal lobe interictal epileptiform discharges (group with frontal IEDs) and those with seizures originating outside the frontal or temporal lobes (group with extrafrontal IEDs). Sixty healthy individuals served as controls.

Results: The group with frontal IEDs achieved the most severe deficits in emotion recognition, ToM, and cognitive empathy, while affective empathy was intact. Moreover, the performance scores of empathy in the group with frontal IEDs were selectively correlated with their executive function scores, which are believed to be associated with orbitofrontal functioning. In contrast, patients with epilepsies not originating from the frontal or temporal lobes may also be at risk of impairments in social cognition, albeit to a lesser extent.

Conclusions: The preliminary findings suggest that patients with epilepsy, especially those having frontal lobe interictal epileptiform discharges, have associated general social cognition deficits. At the clinical level, these results are in line with previous findings regarding social cognition and the importance of the prefrontal area in the integration of cognition and affect. At the theoretical level, our findings also provide evidence for the functional independence of cognitive from affective aspects of empathy.

1. Introduction

Epilepsy is a common neurological disorder that can be complicated by neurobehavioral comorbidities, which include cognitive impairment, psychiatric disorders, and social problems [1]. Patients with epilepsy may experience communication problems and interpersonal difficulties, and they face negative emotional and psychosocial consequences such as poor social adjustment, emotional impairment, and problems in daily activities [2], which have significant bearing on quality of life [3]. Neuropsychological studies of individuals with epilepsy have not demonstrated a specific pattern of impairment. Nonsocial cognitive functions including memory, language, and attention deficits have been studied for many years, whereas social cognitive abilities have received little attention [4]. Because social cognition is a broad concept, less is known about the integrity of social cognition in individuals with epilepsy. The cognitive and behavioral disturbances in epilepsy are consequences of a range of multifaceted and overlapping influences, and different levels and subcomponents of social cognition could be differentially impaired. Further research that explores the connections between them and their relationships with epilepsy is required.

Social cognition has been defined as the ability to interpret and predict others' behavior based on their beliefs, feelings, and intentions and to interact in complex social environments and relationships around us [5]. It guides both automatic and volitional behavior. Social cognition is composed of a variety of cognitive, emotional, and motivational processes, which modulate behavioral responses that enable us to engage in the activities we value most [6]. Accordingly, impairments in social cognition appear to contribute to social adaptive and communicative impairments characteristic of individuals with several psychiatric

* Corresponding author. Tel./fax: +86 551 2923704.
E-mail addresses: calottriangle@126.com (Y. Hu), jiangyubao1982@126.com (Y. Jiang), hpppanda9@126.com (P. Hu), maer0719@126.com (H. Ma), wangkai1964@126.com (K. Wang).

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disorders, such as autism [7], schizophrenia [8], and alcoholism [9], as well as neurological conditions, such as traumatic brain injury [10], frontotemporal dementia [11], and lesions especially in the frontal lobe [12], that are accompanied by different types and subcomponents of deficits in social cognition. Experiments using imaging techniques and studies on patients with brain injuries have found underlying neural processes localized to different brain regions, particularly the frontal region [13,14].

The recognition of emotional signals, especially in faces, is a critical component of human social interactions because it is our understanding of the affective states of others that guides our behavioral responses [15]. Facial expressions convey important information about the internal states of others and the external events that may have elicited those expressions. At a more sophisticated level, the most representative mechanism of social cognition is Theory of Mind (ToM), which alludes to a skill that underlies humans' ability to engage in complex social interactions [16]. We constantly make assumptions about the intentions and beliefs of others, which form the framework of our complex interpretations of human behavior in daily life. These mentalistic interpretations represent a fundamental aspect of social cognition, which has been coined ToM [17]. Recently, social cognitive neuroscience has begun to define subcomponents of the complex concept of ToM. One important differentiation is that of cognitive versus affective ToM. Cognitive ToM refers to the ability to make inferences about the cognitive states, thoughts, intentions, and motivations of other people (knowledge about beliefs), while affective ToM refers to the ability to infer the feelings, affective states, and emotions of others (knowledge about emotions) [18]. These cognitive and affective aspects of ToM raise the question of the relationship between ToM and another aspect of social behavior, namely "empathy", which is a multifaceted phenomenon broadly defined as our reaction to the observed experiences of others [19]. Similar to ToM, recent evidence supports a model of 2 separate systems for empathy: a cognitive system and an emotional system. The term "cognitive empathy" describes empathy as a cognitive role-taking ability or the capacity to engage in the cognitive process of adopting another's psychological point of view. On the other hand, the capacity to experience affective reactions to the observed experiences of others or share a "fellow feeling" has been described as "affective empathy" [20]. Currently, there is no clear distinction between empathy and the ToM concept, leading some researchers to use these terms interchangeably [21]. Both rely on networks associated with making inferences about mental states of others [22]. It appears that the centrality of emotion distinguishes the cognitive and affective aspects of ToM and empathy [21].

The advent of social neuroscience within the last decade has provided tests and paradigms that may help to reveal the underlying deficits responsible for social maladaptive behavior in clinical populations [23]. To date, only a few studies have looked at the relationship between cognitive or affective empathy and cognitive and affective ToM in patients with epilepsy [24]. Thus, it is not clear whether these terms are related. There is also some evidence that ToM, which is closely related to the cognitive component of empathy, is affected in people with epilepsy [24,25]. However, few studies have demonstrated impaired empathy or lower levels of social perspective-taking ability in patients with epilepsy [26,27]. Therefore, to understand more fully the different components of social cognition in people with epilepsy, we investigated social cognitive functions in patients with epilepsy using a variety of tests involving empathy and ToM in different modalities, as well as emotion recognition and the relationships between these tasks. Considering that ToM and empathy can be divided into at least 2 subcomponents (cognitive and affective) with different neural bases, patients with epilepsy with interictal epileptiform discharges (IEDs) originating from different areas of the brain offer a crucial contribution to the study of this function. Because previous studies have indicated that the prefrontal cortex (PFC) mediates affective information, emotional stimuli, and social behavior [28,29], we hypothesized that patients with interictal epileptiform discharges in the frontal lobe (frontal IEDs) would achieve lower scores on social cognitive tasks compared with patients with epilepsy not originating from the frontal or temporal lobes (extrafrontal IEDs) and healthy controls (HC). Furthermore, we explored whether there were dissociable patterns of deficits in empathy in people with epilepsy and the relationship between different components of social cognition. To the best of our knowledge, no previous studies have examined the relationships between these complex social cognition tasks in patients with interictal epileptiform discharges.

2. Materials and methods

2.1. Participants

All patients (age range: 12–25 years) were recruited from the clinic for epilepsy of the First Affiliated Hospital of Anhui Medical University, Anhui Province, China. A total of 53 right-handed patients (30 male and 23 female) with IEDs qualified and agreed to participate in the study. In addition, a good knowledge of the Chinese language and a confirmed diagnosis of epileptic seizures were required. Patients with concomitant neurological problems (e.g., hemiplegia, tumors, head injury, and diseases of the CNS), previous brain surgery, or psychiatric disorders were excluded. Additional exclusion criteria were the Montreal Cognitive Assessment (MoCA) scores below 26 (representing intellectual impairment) and fewer than 6 years of education. Patients with a diagnosis of temporal lobe seizures were excluded from the study to rule out functional involvement of this area in social cognition. Finally, patients with adjustment disorders, moderate depression, or anxiety were also excluded from this study since it was assumed that social cognition impairments may be related to psychiatric disorders [30]. All patients underwent a detailed clinical and neurological examination, continuous ambulatory 24-hour EEG monitoring, and high resolution MRI. Lateralization and localization were based on lesion site as determined by EEG investigations. Patients recruited were on their usual antiepileptic regime such as sodium valproate, carbamazepine, or lamotrigine, and none of the patients experienced a seizure in the 24-hour period preceding the experimental session. On this basis, 10 patients were classified as the group with frontal IEDs, and 43 patients were in the group with extrafrontal IEDs. All patients were diagnosed according to the International League Against Epilepsy criteria [31]. The group with extrafrontal IEDs served as the clinical control group.

The control group included 60 healthy right-handed volunteers with average achievements in regular schools and the communities, who were chosen at testing to match patients with respect to age, sex, and years of education. They all had normal vision and hearing and were able to understand the experimental procedures. None of the participants had any current or previous serious medical or neurological condition.

The study was approved by the local ethics committees, and all participants gave informed consent prior to their inclusion in the study.

2.2. Background neuropsychological and behavioral assessment

A background neuropsychological test battery was used to measure various aspects of cognition, including intelligence, memory, language, executive function, depression, and anxiety in the patients and control participants. All patients completed the MoCA [32] to estimate general intellectual functioning. Executive functions were assessed by verbal fluency (category: animals, fruit, and vegetables) [30]. Subjects were asked to report as many items as possible within each category in 60 s. Furthermore, the Stroop test [33] was also administered by reading 3 pieces of paper written with different colors and recording the time. The digit span test [34] was performed to assess working memory, executive function, and attention span. The subject was asked to recall the numbers in ascending numerical order (forward) or reverse numerical order (backward). In addition, all participants filled out the Beck