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Theory of Mind impairment in focal versus generalized epilepsy

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ABSTRACT

Theory of Mind (ToM) is a critical component of social cognition, and thus, its impairment may adversely affect social functioning and quality of life. Recent evidence has suggested that it is impaired in epilepsy. What is not clear, however, is whether it is related to particular types of epilepsy or other factors. We undertook the present study to explore ToM in patients with focal versus those with generalized epilepsy, the particular pattern of ToM deficits, and the potential influence of antiepileptic medication load. Our sample included 149 adults: 79 patients with epilepsy (34 with generalized epilepsy and 45 with focal epilepsy) and 70 healthy controls. Theory of Mind tasks included a) comprehension of hinting, b) comprehension of sarcasm and metaphor, c) comprehension of false beliefs and deception, d) recognition of faux pas, and e) a visual ToM task in cartoon form. We found significant ToM impairment in the group with focal epilepsy relative to the performance of both the healthy group and the group with generalized epilepsy on all tasks, with the exception of faux pas, on which the group with generalized epilepsy also performed more poorly than the healthy group. Additionally, early age at seizure onset, but not antiepileptic drug (AED) load, was associated with ToM performance. Our findings suggest that focal temporal and frontal lobe, but not generalized, epilepsies were associated with impaired ToM. This may reflect the neuroanatomical abnormalities in the relevant neuronal networks and may have implications for differential cognitive-behavioral interventions based on epilepsy type.

1. Introduction

Emerging evidence of Theory of Mind (ToM) impairment among individuals with epilepsy has highlighted the importance of including such an exploration in routine assessments of patients' cognitive and social functioning. Theory of Mind refers to the ability to put oneself in the perspective of another person and to infer his/her mental state as potentially different from one's own [1,2]. It is an essential component of social functioning and interpersonal interactions. If impaired, it may have a negative impact on quality of life.

Social cognition in generalized epilepsy has received limited research attention to date as compared with other disorders. Previous reports [3,4] have shown moderate ToM abilities in patients with generalized epilepsy relative to healthy participants or individuals with focal (specifically temporal lobe) epilepsy. Patients with generalized epilepsy have been found to have either normal faux pas (FP) recognition [3] or performance between that of patients with focal epilepsy on FP and emotion recognition, as well as on intention attribution tasks [4]. In line with these findings, additional studies [5,6] have demonstrated that ToM abilities in patients with generalized epilepsy were impaired in anger and fear recognition only but displayed almost intact intention and emotion attribution abilities with scores again between those attained by the healthy group and group with temporal lobe epilepsy. In contrast, Jiang and colleagues [7] observed ToM deficits in patients with generalized epilepsy patients, specifically concerning eye emotion recognition and cognitive empathy abilities with intact affective empathy.

Theory of Mind impairment in both temporal [8] and frontal lobe epilepsies has received considerable empirical attention [9,10]. Patients with mesial temporal lobe epilepsy have demonstrated severe deficits in FP recognition relative to patients with generalized epilepsy and extramesial temporal lobe epilepsy [3,4,11] despite normal performance on face recognition [4]. Moreover, investigations of patients with temporal lobe epilepsy have also reported deficits in emotional intelligence, facial emotion recognition, and deceitful and sarcastic speech comprehension in social exchanges [12,13]. Indeed, Wang and colleagues [14] described extensive impairment in both basic and advanced ToM functions (i.e., FP/false belief recognition, mental state inference) in a group with temporal lobe epilepsy. Additionally, FP recognition deficits were observed in patients with cryptogenic epilepsy

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[15], but the same research group found no ToM impairment in patients with temporal lobe epilepsy in a subsequent study [11].

Given the role of the frontal lobes in aspects of social cognition, researchers have also explored ToM in patients with frontal lobe epilepsy [16]. In particular, Farrant and colleagues [17] described impairment in the Reading the Mind in the Eyes task, humor appreciation, and emotion recognition tasks but normal performance on FP and "Happe's strange stories" in patients with frontal lobe epilepsy. Happe's strange stories is a task that involves the comprehension of nonliteral statements in hedged expressions, metaphors, irony, lies, sarcasm, and first and second order deception. On the other hand, subsequent studies [11,18] reported significant FP deficits in patients with frontal lobe epilepsy. Other researchers [19] have also observed significant impairment in the Yoni task (which assesses cognitive and affective ToM abilities based on verbal cues, eye gaze, and facial expressions) and cognitive empathy despite intact affective empathy.

Furthermore, additional explorations have revealed a relationship between ToM impairment and clinical variables in patients with focal epilepsy [16]. Seizure-related factors demonstrating the strongest associations with poor ToM performance were early age of seizure onset, disease duration, and the number of antiepileptic drugs (AEDs) taken. Moreover, findings pointed to indications of neurodevelopmental injury (e.g., dysembryoplastic neuroepithelial tumor and mesial temporal lobe sclerosis) [11,16]. Thus, clinical features related to focal epilepsy have been found to adversely affect ToM performance.

Given the role of the amygdala in ToM processing, some studies have explored ToM in mesial temporal lobe epilepsy associated with amygdala damage. These studies have yielded conflicting findings, perhaps reflective of the acute or early manifestation of the damage. For example, Shaw and colleagues [20] observed that patients who underwent amygdalectomy showed no postoperative change in their ToM performance but demonstrated improvement in the recognition of fear in facial expressions approaching normal levels. Indeed, the role of the amygdala in higher level ToM has been supported in studies of patients with congenital or early amygdala damage, whose ToM abilities were impaired in detecting "socially incomplete" (FP task) or sarcastic speech, recognition of second order false beliefs, understanding of another's motivation, and the interpretation of nonverbal emotional expressions [21,22]. Thus, the amygdala appears to play a role in the development of the neural circuitry mediating ToM.

Our goal in undertaking the current research study was to investigate potential differences in ToM between patients with generalized epilepsy and those with focal epilepsy (specifically temporal and frontal lobe epilepsies), expecting that damage specifically to temporal and frontal regions would lead to greater and more extensive ToM impairment than in cases with presumably generalized or diffuse damage. We also sought to explore the potential influence of clinical features namely age of seizure onset and illness duration, as well as AED load on ToM performance, expecting that these variables would further compromise ToM.

2. Methods

2.1. Participants

A total of 79 patients with different epilepsy syndromes were recruited for the study. The patients had been diagnosed or were being treated over a 36-month period in the epilepsy monitoring units of two neurology clinics at Papanikolaou and AHEPA Hospitals in Thessaloniki, Greece. Clinical diagnosis for the selected cases (n = 79) was supported by electroencephalography (EEG) recordings, followed by magnetic resonance imaging (MRI) scans (n = 71). We studied these clinical data in order to determine the localization and the etiology of the epileptic seizures (lesion localization and type). Thirty-five of the patients had a diagnosis of generalized epilepsy (group with generalized epilepsy: nine with juvenile myoclonic epilepsy, seven with juvenile absence epilepsy, and 19 with other types of generalized epilepsy), 30 with temporal lobe epilepsy (group with temporal lobe epilepsy: 12 with right and 11 with left hemisphere loci), four with frontal lobe epilepsy (group with frontal lobe epilepsy), seven with focal lesions originating in areas other than the frontal and temporal lobes (e.g., occipital regions), and three with an undefined type of epilepsy. Magnetic resonance imaging scans indicated unilateral hippocampal sclerosis in 12 of the patients with temporal lobe epilepsy (eight in the right hemisphere, three in the left hemisphere, and one bilateral). Those patients with focal lesions outside the frontal and temporal lobes as well as those with an undefined type of epilepsy were excluded from the statistical analyses. We also excluded patients with a history of psychiatric illness (e.g., psychosis), developmental disorders related to intellectual deficits, or other physical diseases which could have caused mental impairment. We did not exclude patients with medically treated anxiety or depression as these conditions are frequent comorbid symptoms of epilepsy. Also, we did not exclude patients based on medical comorbidity as most additional diagnoses did not involve the functioning of the central nervous system and they were equally dispersed between the two patient groups.

The healthy control group consisted of 70 healthy participants, who had no history of a neurological or a psychiatric disorder and received no treatment. The patients with generalized epilepsy served as a patient control group; they were comparable with the group with focal epilepsy with respect to AED load and had not had daily seizures for at least a six-month period or their seizures were rare. The seizure frequency for each patient was classified into one of three categories (I. daily seizures — one or more seizures per day, II. persistent seizures — less than one per day but at least one per six months, and III. rare or no seizures — less than one per six months) based on Lüders' classification system [23]. For the purposes of the present study, patients with frontal and temporal lobe epilepsies were combined to form a single group with focal epilepsy, comprising only focal epilepsy syndromes involving the neural network related to ToM. The three groups (healthy control, generalized, and focal epilepsy) were matched on level of education [$F(2, 113) = 2.423$, $p = .093$] but differed with respect to gender ratio [there were more men than women in the healthy control group but the reverse pattern in both groups with epilepsy; $\chi^2(2) = 15{,}078$, $p = .001$] and age [$F(2, 113) = 6.249$, $p = .001$; patients with focal epilepsy were significantly older than those in the healthy control group and group with generalized epilepsy; the latter two groups did not differ in age]. Since we found a significant correlation between age and ToM scores, we employed age as a covariate in the statistical analyses. Gender was not associated with ToM performance. Table 1 summarizes the demographic characteristics for all groups as well as the clinical data for the patient groups. All participants gave written informed consent to participate in the study and were treated in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.2. Procedure

Participants were informed about the nature of the study and agreed to participate. They then completed a series of tasks examining verbal and visual ToM, as well as emotion recognition. The tasks were administered individually to the participants and took about 1–1.5 h to complete. The administration order of the tasks differed systematically for each participant so as to eliminate possible order effects. Specifically, we applied a pseudo-randomized administration order with two delivery options. For this purpose, tasks were divided into two parts: part A consisted of the visual ToM task while part B comprised the verbal ToM tasks in the following order: hinting task, sarcasm and metaphor task, false belief, FP, and deception scenarios. We switched the delivery order of the two parts to the participants alternately so that for each participant, test category order was different as compared with the previous and the next one. As a result, half of the participants were