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Facial emotion recognition in childhood: The effects of febrile seizures in the developing brain

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ABSTRACT

It has been documented that anteromedial temporal lobe dysfunction can cause impairment in emotional intelligence. In particular, medial temporal lobe epilepsy (MTLE) is associated with disorders in emotion recognition from facial expressions. About one-third of patients with MTLE experienced febrile seizures (FSs) during childhood. In the present study, we investigated facial emotion recognition ability in a group of 38 school-aged children with antecedent FSs and in an age- and sex-matched control group. Children with abnormal general visuoperceptual abilities were excluded. Children with FSs showed lower recognition scores versus controls in both matching (28.64 vs 33.47; $p < .0001$) and labeling (21.25 vs 23.03; $p = .001$) facial emotions. Our findings support the hypothesis that FSs can be associated during childhood with a dysfunction within the neural network subserving the processing of facial expressions of the basic emotions.

1. Introduction

Febrile seizures (FSs) are the most common seizure disorder in childhood associated with fever but without evidence of intracranial infection or defined causes [1]. They occur in 2–5% of children younger than 5 years of age, and based on duration and clinical features, FSs are subdivided into 'simple' and 'complex' [1,2]. Epidemiological studies have substantially improved our understanding of the frequency, natural history, and recurrence of FSs, and there is now a general agreement that simple FSs are benign and rarely require chronic anticonvulsant treatment. Recent clinical and genetic studies suggest that the relationship between FSs and the development of epilepsy later in life is frequently genetic, and there are a number of genes that are either involved in susceptibility for FSs [3] or are pathogenic in epilepsies that present with FSs in their course [4,5]. However, the impact of FSs on the developing brain has not been completely understood. Since FSs are the most common seizures in children, it is important to delineate whether early-life FSs can alter long-term neuroplasticity [6], especially the cognitive functions. In particular, it is important to evaluate whether FSs could be linked to persistent subtle brain injuries and the related cognitive dysfunctions. Regarding anatomical injury, longitudinal MRI studies have documented that prolonged and focal FSs can occasionally produce acute hippocampal injury that evolves into atrophy [7–9]. On the other hand, it has been proposed that a preexisting developmental hippocampal abnormality may predispose individuals to having a prolonged febrile seizure [9,10]. Indeed, the association between hippocampal sclerosis and FSs raises the possibility of selective cognitive sequelae involving the cognitive functions subserved by the medial temporal lobe region. In early reports from hospital-based studies, the prognosis of FSs, in terms of cognitive outcome, was fairly pessimistic (8% to 22% of cases presented mental retardation) because of the inclusion of symptomatic causes of seizures other than fever [11]. Furthermore, the hospital-based studies may be skewed toward disproportionately severe cases [12]. In contrast, long-term population-based cohort studies showed that children with FSs have similar global neurocognitive

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developmental and academic performance compared with controls [13–16]. Therefore, the current viewpoint is that the vast majority of children with FSs have normal global measures of cognition and behavior. However, previous studies on the outcome of children with FSs only rarely focused on specific cognitive functions that can reveal a FS-related hippocampal injury, such as memory [17].

Neural networks underlying facial emotion recognition involve a distributed set of structures that include the visual cortices, the amygdala, the orbitofrontal cortex, and additional cerebral regions, such as the insula, the basal ganglia, and the prefrontal cortex [18]. The amygdala, which is often damaged along with the hippocampus in patients with medial temporal lobe epilepsy (MTLE) [19], has been identified as a key structure for evaluating emotional stimuli and regulating social and emotional behavior [20–22]. Accordingly, the investigation of emotional and social competences in patients with MTLE has been the focus of different studies [23–32] documenting common and widespread deficits of emotion recognition in this seizure disorder. In particular, patients with early onset of seizures, including FSs, and bilateral medial temporal lobe damage were severely impaired in emotion recognition [23,30,33]. The recognition of emotional signals, from all sensory modalities, is a critical component of human social interactions because it is through the understanding of the affective states of others that we modulate our behavioral responses [34]. Notably, facial expressions provide the greatest amount of emotional cues for recognizing emotions, both with positive and negative values [35]. The expression of basic emotions is supposed to be universal, innate, and have a specific neural substrate; on the contrary, the recognition of social emotions is learned over a lifetime. Thus, the alteration of emotional and social competences could represent another index of the potential FS-related medial temporal lobe injury. To the best of our knowledge, no study has investigated emotional–social abilities in children with antecedent FSs.

In the present study, we assessed the ability of school-aged children with a history of FSs to recognize the facial expressions of basic innate emotions (happiness, sadness, fear, anger, and disgust) [36] in order to explore the possibility that FSs are associated with (or can lead to) a dysfunction within the neural network subserving the processing of facial expressions of basic emotions. Accordingly, we investigated facial emotion recognition (FER) ability in a sample of healthy school-aged children with antecedent FSs and compared their performances with an age- and sex-matched control group.

2. Material and methods

2.1. Participants

We reviewed the database from the Child Neuropsychiatry Unit of the University-Hospital of Parma (Italy) to recruit children referred to our service between 2000 and 2008 for FSs, who were school-aged at the time of the enrollment. Following the International League Against Epilepsy [37], a FS was defined as a seizure occurring between 1 month and 5 years of age, associated with a febrile illness but not caused by an infection of the CNS, without previous neonatal seizures or a previous unprovoked seizure, and not meeting the criteria for other acute symptomatic seizures. Accordingly, we selected only cases with a complete diagnostic workup, including detailed eyewitness accounts of the episodes, clinical course, neurological evaluation, and an EEG recording within 48 h after the FS.

Out of 163 eligible subjects aged 6–10 years, with at least one episode of FS and without subsequent epilepsy, 150 could be contacted, and 25.3% of the children's parents accepted to participate. Thus, 38 children (18 females, 20 males) were recruited as the clinical group (FS group). A group of 38 age- and sex-matched children (18 females, 20 males), attending primary school from the same district, served as the control group (CTRL). All participants' parents gave their informed consent, and the study was approved by the local ethical committee. Demographic and clinical variables were collected through a semistructured interview of parents to explore the children's handedness, educational level, and familial and personal history. A history of neurological and/or neuropsychiatric antecedents was an exclusion criterion for children to be enrolled in the control group. The presence of EEG abnormalities, for the FS group, was evaluated. Demographic variables of the two groups are reported in Table 1; neither the age at the time of testing (ANOVA) nor gender and handedness distributions (chi-square test) were significantly different between groups. For the FS group, the characteristics of FSs were reported, in order to be classified as 'simple' or 'complex' [2,38,39], along with the age at the first episode and the number of episodes (see Table 1). Twenty-one out of 38 (55.3%) children experienced a single episode, more than 80% (31/38) of episodes were classified as simple, and only seven patients experienced at least one episode classified as complex, being focal (4/38) and/or prolonged (4/38) and/or drug-interrupted (2/38). Half of our FS group (19/38) experienced only a single, simple, and short FS.

2.2. Neuropsychological assessment

The children's IQ was evaluated by means of Raven's colored progressive matrices (CPM) [40]. The experimental protocol included three tasks built ad hoc with Ekman and Friesen's Pictures of Facial Affect [41] depicting five emotional expressions (happiness, sadness, fear, disgust, and anger) or no emotion (neutral). Ekman and Friesen's Pictures of Facial Affect represent a validated and reliable set of posed emotional expressions that generate high recognition rates across cultures; accordingly, they have been used in a wide range of studies, including developmental, cross-cultural, neuroimaging, and behavioral studies [42,43]. These black and white pictures were initially developed and used with adults, but they were later fruitfully implemented in studies with children [42]. Facial stimuli expressing surprise were not included because the intrinsic ambiguity of this emotion led some authors to consider it not among the basic emotions [43] or to consider it a 'gradation' of fear [44], and even healthy subjects often confuse fear for surprise [45]. The original stimuli were digitally edited in order to remove all nonface cues (i.e., clothing, neck, and hair).

2.2.1. Face Identity Matching Test

Neutral stimuli from 10 subjects (five males) were used to create the Face Identity Matching Test (FIMT), aimed to control for subjects' basic visuoperceptual ability with facial stimuli. In this task, the children were required to identify the target face, portrayed in the upper half of the page, among five alternatives (one target and four confounders) depicted below (Fig. s-1A, online supplementary material).

2.2.2. Facial Expression Matching Test

The second task, the Facial Expression Matching Test (FEMT), was created to assess FER ability, and it did not require any verbal expertise. This test comprised 40 emotional items in which the probe facial expressions resulted in a high rate of correct identification in the adult data [41]. All stimuli were faces of four women (C, MF, MO, and MR in the Ekman and Friesen's series) and four men (EM, GS, JJ, and WF) depicting the five basic emotions. For each item, the subjects were requested to match the probe facial expression with one of the five alternatives aligned below. The targets and confounders were expressions of the same actor, while the probe expression belonged to a different actor of the same gender (Fig. s-1B). The probe emotion and gender, as well as the position of the target among the confounders, varied across subsequent items in a pseudorandom sequence in order to minimize repetitions (see Table s-1, online supplementary material).

2.2.3. Facial Expression Labeling Test

This test was already used in previous studies from our group to quantify the FER ability of adult subjects [23,30,31]. Briefly, in this task for each trial, the subject was presented with one original stimulus from Ekman and Friesen's series (including nonfacial features) and