European Journal of Paediatric Neurology 28 (2020) 167–175

Contents lists available at ScienceDirect

European Journal of Paediatric Neurology

Social cognition and executive functions in children and adolescents with focal epilepsy

Francesca Felicia Operto [a,*], Grazia Maria Giovanna Pastorino [a,b], Roberta Mazza [c], Carlo Di Bonaventura [d], Rosa Marotta [e], Nazareno Pastorino [f], Sara Matricardi [g], Alberto Verrotti [h], Marco Carotenuto [b,1], Michele Roccella [i,1]

[a] Child Neuropsychiatry Unit, Department of Medicine, Surgery and Dentistry, University of Salerno, Salerno, Italy
[b] Department of Mental Health, Physical and Preventive Medicine, Clinic of Child and Adolescent Neuropsychiatry, Università degli Studi della Campania "Luigi Vanvitelli", Naples, Italy
[c] Child Neuropsychiatry Unit, Department of Basic Medical Sciences, Neuroscience and Sense Organs, University of Bari "Aldo Moro", Bari, Italy
[d] Epilepsy Unit, Department of Neurosciences/Mental Health, "Sapienza" University, Rome, Italy
[e] Department of Health Sciences, University "Magna Graecia", Catanzaro, Italy
[f] Department of Cultural Heritage Sciences, University of Salerno, Salerno, Italy
[g] Department of Pediatrics, University of Chieti, Chieti, Italy
[h] Department of Pediatrics, University of L'Aquila, L'Aquila, Italy
[i] Department of Psychological, Pedagogical and Educational Sciences, University of Palermo, Palermo, Italy

ARTICLE INFO

Article history:
Received 5 December 2019
Received in revised form
23 June 2020
Accepted 24 June 2020

Keywords:
Social cognition
Theory of mind
Executive function
Epilepsy
Children
Adolescents

ABSTRACT

Objectives: Deficits in facial emotion recognition and Theory of Mind are frequent in patients with epilepsy. Although this evidence, studies on pediatric age are few and the relation between these abilities and other cognitive domain remains to be better elucidated. The purpose of our study is to evaluate facial emotion recognition and Theory of Mind in children and adolescents with focal epilepsy, and correlate them with intelligence and executive functions.
Materials and methods: Our work is a cross-sectional observational study. Sixty-two children and adolescents aged between 7-16 years diagnosed by focal epilepsy and 32 sex/age-matched controls were recruited. All participants were administered a standardized battery tests to assess social cognition (NEPSY-II), executive functions (EpiTrack Junior) and cognitive non-verbal level (Raven Progressive Matrices).
Results: Emotion recognition mean score was significantly lower in the epilepsy group than in the controls to Student's t-test ($p<0.05$). Epilepsy group showed an impairment in happiness, sadness, anger and fear recognition, compared to controls ($p<0.05$). Theory of Mind mean score was also significantly lower in epilepsy group than controls ($p<0.05$). Deficits in emotion recognition seemed to be related to low age at onset of epilepsy, long duration of disease, low executive functions and low non-verbal intelligence. Deficits in Theory of Mind seemed to be related to a high seizure frequency.
Conclusions: Our results suggest that children and adolescents with focal epilepsy had deficit in facial emotion recognition and Theory of Mind, compared to their peer.
Both these difficulties seem to be related to some features of epilepsy itself. Our results also suggest that deficits in facial emotion recognition are potentially related to difficulties in executive functions and non-verbal intelligence. More studies are needed to confirm these hypotheses.

1. Introduction

Social cognition (SC) has been defined as the ability to understand, interpret, and respond appropriately to social cue, in order to better interact with external world [1,2]. In this perspective, SC is crucial for adaptive functioning and good quality of life, and its

* Corresponding author. Child and Adolescent Neuropsychiatry Unit, Department of Medicine, Surgery and Dentistry, University of Salerno, Via Salvator Allende, Via Allende, 84081, Baronissi, SA, Italy.
E-mail address: opertofrancesca@gmail.com (F.F. Operto).
[1] equal contribution.

https://doi.org/10.1016/j.ejpn.2020.06.019
1090-3798/

deficits can significantly contribute to psychosocial difficulties in both children and adults [3,4].

Deficits of social cognition have been typically highlighted in children and adults with Autism Spectrum Disorder, but also in other neurodevelopment disorders (Attention Deficit/Hyperactivity Disorder, Specific Learning Disorders) or epilepsy [5–7].

SC includes basic decoding abilities (e.g. facial emotion recognition, prosody perception) as well as higher-order skills that allow each subject to infer thoughts, intentions, belief, and desire of others and understand and predict others' behaviour based on their mental states (e.g. Theory of Mind, empathy, moral reasoning) [8,9].

Facial emotion recognition is the ability to identify accurately face emotional expression. There are some innate emotions universally identifiable by humans, such as happiness, sadness, anger, fear and disgust [10]. The ability to recognize these emotions, together with neutral facial expressions, develops gradually from childhood to adolescence: the first emotion identified is happiness, followed by negative emotions, such as fear, anger and disgust [11]. Neural networks underlying this ability involve a set of structures that includes the visual cortex, the orbitofrontal cortex, the insula and the basal ganglia but mainly the medial temporal structures, with an important role played by amygdala [12]. In normal development, the neural networks for facial emotion recognition also mature progressively, from early childhood until the end of adolescence [13,14].

Theory of Mind includes the capacity to understand mental states and beliefs (cognitive Theory of Mind) as well as emotional states of the others (affective Theory of Mind).

In typical developing children, this complex ability emerges during preschool years, around the age of 3–4, and continues to refine with adolescence until adulthood, first emerging with a basic understanding of belief and extending to understandings more advanced of both cognitive and affective states [15]. The neural network underlying Theory of mind ability is more complex. Neuroimaging and lesion studies have shown the involvement of a widespread network of prefrontal, temporoparietal and mesolimbic brain structure [16,17].

Since both, facial emotion recognition and Theory of Mind abilities, gradually improve during childhood and adolescence, it is important to consider that different factors, such as epileptiform activity, can affect their development.

Several studies have highlighted that the deficit in social cognition are common in people with epilepsy, and an early onset of crises is related to greater difficulties [18]. Indeed, early-onset epilepsy could affect the plasticity and the maturation of neural networks in a critical period of life, both due to the seizures themselves and as a consequence of the potential associated lesions. The clear overlap between the neural networks involved in temporal and frontal lobe epilepsies and the social cognitive neural network, offers a plausible physiological basis for these deficits [19]. Neuroimaging studies suggested that the right medial temporal lobe is primarily involved in the processing of fear, but that related lesions disrupt the overall neural network involved in social cognition. Similarly, localized amygdala lesions altered the functional activation pattern in distal regions of the entire social cognition network [20]. In this regard, some studies of Meletti et al. suggested that an early-onset right medial temporal lobe epilepsy could play a crucial role in causing facial emotion recognition impairment in adults [21,22].

Furthermore, deficits in Theory of Mind are common also in children with epilepsy [23,24]. A very recent review shows significant impairment in both facial emotion recognition and Theory of Mind among children and adolescents, which did not seem to differ in focal or generalized epilepsy, in line with the new understanding of epilepsy as a network disease. Results show, also in this case, that age at seizure onset and duration of epilepsy could be related to severity of these deficits [7].

Another important aspect to consider is the interaction between social cognition and executive functions (EF). EF are high-level processes supporting flexible behavior, adaptation to novel context and inhibition of stereotyped responses. They include basic cognitive abilities such inhibitory control, working memory, and cognitive flexibility. From these, higher-order EFs are built such as problem solving, and planning [25].

Executive functions gradually develop and change across the lifespan. Inhibitory control and working memory are among the earliest EF to appear, with initial signs around 12-months of age. Then, between the ages of 3–5 years, cognitive flexibility and planning begin to develop. Higher-order EFs develop and growth over pre-adolescence and adolescence.

Several authors suggest a potential association between SC and EF, but it is not clear whether they are distinct and functionally related abilities, or rather representative of a unitary process. the exact nature of this relationship remains unclear, three theories remain ongoing areas of debate: the first theory provides that EF abilities, such as self-monitoring and inhibitory control, are necessary to SC development, (e.g., understand the mental states of oneself and others); conversely, the rationale behind the second theory is that the emotion recognition and the understanding of mental states of the others are required in order to strategically control thoughts and behavior; finally, the theory of a "common neural basis" between SC and EF was initially made by researchers examining the etiology of autism and its associated neurocognitive dysfunctions. Concomitant deficits in both SC and EF in these children led to consider a common neural architecture, particularly involving prefrontal cortical regions, supporting both of these cognitive abilities [26–28].

An additional point to consider is the relationship between SC and cognitive abilities. From a neuroscience perspective, the different stages of the emotion recognition process are based on multiple intelligence components: at the first stage, sensory information is extracted and encoded, requiring perceptual abilities: at the second stage, this information is integrated with existing representations, drawing on fluid non-verbal abilities, crystallized ability, and long-term memory; finally, information need to be maintained in the working memory [12,29].

Several studies have provided evidence of a more or less strong relationship between intelligence and emotional abilities. In particular, it is observed that individual's emotion recognition is correlated with fluid non-verbal intelligence (logical reasoning ability, independent of acquired knowledge) that is required to perceive and integrate the numerous and subtle non-verbal stimuli of emotional expression [30]. Schleger et al. (2017) showed that higher fluid intelligence and higher visual sensory sensitivity are important and independent predictors of facial emotion recognition. Higher sensitivity to visual information likely enhances the extraction and encoding of subtle changes in visual cues in the early stages of the emotion recognition process. In later stages, higher fluid intelligence might facilitate the integration of the sensory information with existing representations of emotional expressions and the associated knowledge [31].

A very recent meta-analysis of Schleger et al. (2020) provides a comprehensive overview of the association between emotional recognition abilities and basic components of intelligence. Overall, the Authors showed a positive correlation between emotion recognition and intelligence, including visual-spatial ability and fluid non-verbal intelligence [32].

In this article we present the results of a cross-sectional cohort study, investigating facial emotional recognition and Theory of Mind in 62 children and adolescents with epilepsy, compared to age-matched controls. In particular, our aim is to evaluate whether epilepsy and epilepsy-related variable (e.g. age at onset, epilepsy duration, and drug therapy) can affect these abilities. Another aim of our study is to explore the possible correlation of facial emotional recognition and Theory of Mind with non-verbal cognitive abilities and executive functions.

2. Materials and Methods

2.1. Sample selection

Our work is a cross-sectional observational study that aims to explore social cognition (facial emotion recognition and theory of mind) in young patients with epilepsy.

Sixty-two children and adolescents aged between 7 and 16years, with a diagnosis of focal epilepsy, were prospectively recruited at the Child Neuropsychiatry Unit of the University Hospital of Salerno, from December 2017 to September 2019. The diagnosis was established on the basis of the typical clinical semiology of seizures and the EEG findings. The sub-typing of focal epilepsy was made by ictal and interictal scalp EEG characteristics, magnetic resonance imaging (MRI) findings and clinical history.

A control group was also recruited, including 32 healthy children and adolescent. In all patients of the control group the diagnosis of epilepsy was excluded and all had a normal EEG.

All participants in the current study had normal or corrected vision. Epileptic patients and controls were excluded if they had additional neurological (cerebral palsy, intellectual disability, neurodegenerative diseases or migraine), psychiatric (anxiety, depression and psychosis), or other relevant medical conditions (endocrinopathies, metabolic, hepatic, cardiac or renal disorders).

To guarantee the homogeneity of the two groups, the variables age, sex, years of schooling, intellectual level, and level of maternal education have been considered.

Epileptic patients and controls were administered a standardized battery tests by a single child neuropsychiatrist, to evaluate social cognition, executive function and cognitive non-verbal levels.

All participants and their parents were provided to a clear and detailed explanation about the purposes of the study and the procedures involved. Parents provided their informed consent in written form. The procedure was approved by the local ethics committee, according to the rules of good clinical practice, in keeping with the Declaration of Helsinki. Sample characteristics are summarized in Table 1.

Table 1
Demographic and clinical characteristics.

	EPILEPSY GROUP	CONTROL GROUP	STATISTICS
N	62	32	
SEX			
Male	40 (65%)	18 (56%)	$\chi^2 = 0\text{-}610$
Female	22 (35%)	14 (44%)	$p = 0.240$
AGE INYEARS (M ± SD)	12.74 ±3.4	11.78 ±3.87	t = 1.24 $p = 0.219$
YEARS OF SCHOOLING	8.38 ± 3.62	9.45 ± 3.15	t = 1.49 $p = 0.139$
EPILEPSY CHARACTERISTICS			
Age at onset (M ± SD)	6.74 ±3.96		
Epilepsy duration in year (M ± SD)	6.00±4.04		
Probable side of seizure onset			
Left	30 (48%)		
Right	32 (52%)		
Probable lobe of seizure onset			
Temporal	38 (61%)		
Frontal	15 (24%)		
Occipital	9 (15%)		
Seizure frequency (M ± SD)			
Monthly	20 (32%)		
Weekly	26 (42%)		
Daily	16 (26%)		
Drug therapy			
Mono	36 (58%)		
Poli	26 (42%)		
Number of ASDs(M ± SD)	1,6 ±0.78		
MRI positive	16 (26%)		
-Frontal lobe	3 cortical dysplasia		
-Temporal lobe	5 mesial temporal sclerosis 2 cortical dysplasia 6 hypoxic-ischemic damage		

N = sample size; M = mean; SD = standard deviation; ASD = antiseizure drugs; MRI = magnetic resonance imaging.

2.2. Social cognition assessment – NEPSY-II

The Italian version of the NEPSY-II (Korkman, Kirk and Kemp, 2011) is a battery of tests aimed to evaluate neuropsychological development in preschool, school age and adolescence [33,34]. It is composed of 33 tests, that can be administered individually or with the entire battery.

The social cognition abilities are evaluated by tests of discrimination, recognition and contextualization of emotional facial expressions, and by tests of theory of the mind, which assess the ability to understand mental functions such as beliefs, intentions, deceptions and emotions.

- Theory of Mind (TM): in the verbal part, various scenarios were read or figures were shown to the child, then it is asked him to understand other's point of view. In the non-verbal part, is asked to the child to choose the emotional expression appropriate to the mood of a character depicted in certain social contexts.
- Emotion recognition (ER): visually discriminate a series of facial emotional expressions.

The results of both tests are expressed as raw scores, and then converted into age-weighted scores.

The weighted scores are expressed by a numerical scale, with mean = 10 and standard deviation = 3. Age-standardized scores are classified as follows: ≥8 = normal range; ≤7 = at the lower limits of the norm (-1SD); ≤4 = below the norm (-2SD).

For the analysis of individual emotions recognition, we have considered the parameter “error number”; in this case, a low error score indicates better performance.

2.3. Executive functions assessment – EpiTrack Junior

EpiTrack Junior is a screening tool for executive functions assessment, that is especially sensitive for monitoring epileptic patients [35,36].

It consists of six subtests (working memory, cognitive flexibility, inhibition, processing speed, verbal fluency, visual-spatial planning) that contribute to determining an age-corrected total score. The maximum age-corrected total score is 49.

A total score below 31 points indicates executive functions impairment, according to the following: 29–30 points = mild impairment; ≤28 points = significant impairment.

2.4. Cognitive assessment –Raven Progressive Matrices

Raven's Progressive Matrices (RPM) is a test typically used in measuring non-verbal intelligence in people ranging from 5-year-old to the elderly [37]. It is available in different forms:

– Standard Progressive Matrices (SPM): The booklet comprises five sets of 12 items each, requiring ever greater cognitive capacity to encode and analyze information.
– Colored Progressive Matrices (CPM): Designed for children aged 5 through 11 years-of-age. This test contains three sets of 12 items.
– Advanced progressive matrices (APM): the advanced form contains 48 items of increasing difficulty. These forms are appropriate for adults and adolescents of above-average intelligence.

All participants performed SPM form. Raw scores were converted into percentiles (pc) and age-weighted scores with mean = 100 and standard deviation = 15. Scores <5° pc or <70 are considered under the norm [38].

2.5. Statistical analysis

All neuropsychological scores were expressed as mean ± standard deviation. The percentage of participants scoring lower than expected was also evaluated. A preliminary normality test was carried out in order to verify the data distribution (Kolmogorov-Smirmov Normality Test). The data with a normal distribution (Emotion Recognition, Theory of Mind, EpiTrack Junior and Raven Progressive Matrices scores) were analyzed with parametric statistics methods (t-student test two tailed for independent samples). The data that did not meet the normality criterion (individual emotion error scores) were analyzed with non-parametric statistics tests (Mann-Whitney U test). Multiple regression analysis was performed to evaluate the relationship between Emotion recognition, Theory of Mind, Executive function, Raven Progressive Matrices and epilepsy characteristics. Correction for multiple comparisons was not carried out.

All data were analyzed using the Statistical Package for Social Science, version 23.0 (IBM Corp, 2015); *p* value less than or equal to 0.05 were considered statistically significant.

3. Results

3.1. Sample characteristics

Records of 62 children (N = 24; age <12 years) and adolescents (N = 38; age ≥12 years) with focal epilepsy, and of 32 age/sex matched controls, were included in this study.

All demographic and clinical characteristics of the participants such as age, sex, years of schooling, epilepsy types, seizure frequency, age at onset and duration of epilepsy, probable lobe/side of seizure onset, antiseizure therapy and MRI findings are summarized in Table 1. The two groups did not significantly differ in demographic characteristics (Table 1).

In the epilepsy group 52% of patients had seizure onset in the right hemisphere; 61% of total patients had temporal, 24% frontal and 15% occipital onset.

In the temporal epilepsies group there were 14 children (37%) and 24 adolescents (63%) (mean age = 13.11 ± 3.16). In the frontal epilepsies group there were 5 children (33%) and 10 adolescents (67%) (mean age = 12.60 ± 3.56).In the occipital epilepsies group there were 5 children (56%) and 4 adolescents (44%) (mean age = 11.44 ± 4.16).

3.2. Performance in the epilepsy group and in the control group

Table 2 resumed all neuropsychological mean scores for the NEPSY-II, EpiTrack Junior and RPM in two groups, and the results of statistical comparison.

On NEPSY-IIER (Emotion Recognition) subtest, 26/62 (42%) patients with epilepsy obtained a total score lower than the norm (≤4; <2SD) and 20/62 (32%) patients obtained a total score at the lower limits of the norm (≤7; <1SD), against 0/32 (0%) of controls in both the categories.

The mean ER total score was at the lower limits of the norm for the epilepsy group (mean score = 5.35 ± 2.68; <1SD) while fell into the normal range for the control group (mean score 10.44 ±1.00), and this difference was statistically significant to Student's t-test for unpaired samples ($t(92) = 10.33$, $p<0.00001$).

Analyzing individual emotions, epilepsy group performed significantly lower than control in their abilities to identify happiness, sadness, anger, fear and neutral expressions compared to controls. There was no difference in identification of disgust (see Table 2).

On NEPSY-II TM (Theory of Mind) subtest, 6/62 (9,7%) patients with epilepsy obtained a total score lower than the norm (<4; <2SD) and 38/62 (61%) patients obtained a total score at the lower limits of the norm (≤7; <1SD), respectively against 0/32 (0%) and 4/32 (13%) of controls.

The mean TM total scores was at the lower limits of the norm for the epilepsy group (mean score 6.39± 2.18; <1SD) while fell into the normal range for the control group (mean score 9.69±1.98) and Student's t-test revealed a statically significant difference between the two groups ($t(92) = 7.13$, $p<0.0001$).

With regard to executive functions, the EpiTrack Junior mean score of epilepsy group fell into the "significant impairment" range, while that of the control group fell in the normal range, showing significantly worse performance in the epilepsy group ($t(92) = 4.78$, $p<0.00001$).

In contrast, non-verbal intelligence was conserved in both groups, with mean scores at RPM test falling within the normal range, without statistically significant differences between the two groups ($t(92) = 0.48$, $p = 0.630$).

The multiple regression test analysis, showed some significant relationship in the epileptic group: there was a positive relation between ER score and age of onset of epilepsy ($t = 2.290$, $p = 0.026$) and a negative relation with the duration of the disease ($t = -5.321$, $p<0.001$).Furthermore, the ER score is positively related with executive functions score ($t = 3.464$, $p = 0.001$) and with non-verbal intelligence score ($t = 2.309$, $p = 0.025$). Furthermore, TM score is negatively related with the frequency of seizures ($t = -4.487$, $p<0.001$).No relationship was found between TM and executive functions or non-verbal intelligence scores ($p> 0.05$).

In the control group the multiple regression analysis did not reveal statistically significant relationship between ER or TM and executive functions or non-verbal intelligence ($p>0.05$).

All the results of statistical analysis are summarized in Table 3.

3.3. Comparison between children and adolescents in the epilepsy group and in control group

Both the epileptic group and the control group were further subdivided, according to the age, in a group of children (age<12 years) and in a group of adolescents (age≥12). The demographic characteristics and neuropsychological scores in these subgroups were also statistically examined.

In the epileptic group, children and adolescent did not significantly differ in sex ($\chi^2 = 0.654$, $p = 0.419$), side ($\chi^2 = 0.708$, $p = 0.400$) and lobe (temporal $\chi^2 = 0.144$, $p = 0.704$; frontal $\chi^2 = 1.394$, $p = 0.238$; occipital $\chi^2 = 1.259$, $p = 0.262$) of seizure onset, and MRI positivity ($\chi^2 = 1.708$, $p = 0.191$), seizure frequency ($t(60) = 0.29$, $p = 0.774$), age at onset of epilepsy ($t(60) = 1.87$, $p = 0.066$) and number of ASDs, ($t(60) = 1.46$, $p = 0.149$), but they significantly differed in age of schooling ($t(60) = 9.37$, $p<0.00001$)

Table 2
Performance in social cognition, executive function and cognitive abilities in epilepsy group and control group.

		EPILEPSY GROUP	CONTROL GROUP	STATISTICS
		M ± SD	M ± SD	
SOCIAL COGNITION				
Emotion recognition (ER)	standard score	5.35 ± 2.68	10.44 ± 1.00	Student's t-test t = 10.33, p = 0.000
(single emotions)				Mann-Withney test
Neutral	error number	1.77 ± 1.46	0.84 ± 0.88	U = 593, p = 0.001
Happiness	error number	0.45 ± 0.72	0.16 ± 0.37	U = 785, p = 0.036
Sadness	error number	3.29 ± 1.15	1.44 ±1.80	U = 408, p<0.001
Fear	error number	1.65 ± 1.07	0.50 ± 0.67	U = 373, p<0.001
Anger	error number	2.29 ± 1.45	1.13 ± 1.1	U = 534, p<0.001
Disgust	error number	2.03 ± 0.97	1.67 ± 1.10	U = 777, p = 0.068
Theory of Mind (TM)	standard score	6.39 ± 2.18	9.69 ± 1.98	Student's t-test t = 7.13, p<0.001
EPITRACK JUNIOR	standard score	28.19 ± 4.25	32.22 ± 2.92	Student's t-test t = 4.78, p<0.001
RAVEN PROGRESSIVE MATRICES	standard score	90.48 ± 8.65	91.47 ± 10.44	Student's t-test t = 0.48, p = 0.630

M = mean; SD = standard deviation; p value <0.05 are in bold.

Table 3
Regression analyses.

	EPILEPSY GROUP		CONTROL GROUP	
	ER	TM	ER	TM
EpiTrack Junior	t = 3.464 **p=0.001**	t = 0.108 p = 0.915	t = -0.219 p = 0.828	t = -1.369 p = 0.182
RPM	t = 2.309 **p=0.025**	t = 0.096 p = 0.923	t = -0.822 p = 0.418	t = -0.331 p = 0.743
ER	—	t = 1.958 p = 0.055	t = 1.145 p = 0.262	t = 1.145 p = 0.262
TM	t = 1.958 p = 0.055	—		
Age at onset	t = 2.290 **p<0.001**	t = -0.601 p = 0.550		
Epilepsy duration	t = -5.321 **p<0.001**	t = 1.894 p = 0.064		
Seizure frequency	t = 0.684 p = 0.498	t = -4.487 **p<0.001**		
Lobe of onset	t = -0.913 p = 0.365	t = 0.071 p = 0.943		
Side of onset	t = -1.995 p = 0.051	t = -0.370 p = 0.713		

RPM = Raven Progressive Matrices; ER = emotion recognition; TM = Theory of Mind. p value <0.05 are in bold.

and epilepsy duration (t(60) = 3.69, p<0.0005).

Regarding neuropsychological performances, there was no significant difference between children and adolescents at ER (t(60) = 1.12, p = 0.267), TM (t(60) = 0.63, p = 0.532), EpiTrack Junior (t(60) = 1.53, p = 0.132) and RPM (t(60) = 1.20, p = 0.235) scores. There was no significant difference in the individual emotion recognition, but it was only a trend for significance in identifying fear (U = 330; p = 0.054) and disgust (U = 330; p = 0.053) expression. Mean scores and other statistical analysis are summarized in Table 4.

In the control group, children and adolescent did not significantly differ in sex (χ^2 = 0.097, p = 0.755) but differ in age of schooling (t(30) = 6.84, p<0.00001). There were no significant differences between the two subgroups regarding ER (t(30) = 0.50, p = 0.623), TM (t(30) = 0.40, p = 0.690), EpiTrack Junior (t(30) = 0.50, p = 0.618) and RPM (t(30) = 1.32, p = 0.198) scores.

Regarding the recognition of individual emotions, there were no significant differences in the identification of happiness (U = 122, p = 0.741) and disgust (U = 117, p = 0.670), but children showed significantly lower scores in identifying sadness (U = 50, p = 0.002), fear (U = 81, p = 0.040), anger (U = 62, p = 0.009) and neutral expressions (U = 50, p = 0.002).

4. Discussion

Our study investigated facial emotion recognition and Theory of Mind in children and adolescents with epilepsy, using a battery of standardized neuropsychological test, and correlated it with executive and cognitive functions.

Overall, in keep with previous study, our results show additional evidence that epileptic patients have difficulties in some basic and advanced components of social cognition, such as facial emotion recognition and Theory of Mind, compared to their peers (Fig. 1) [24,39].

In particular, in our sample, children and adolescents with epilepsy have general difficulties in recognizing emotional states through facial expressions, especially as regards sadness, anger, fear and happiness. We also noted tendency to incorrectly attribute certain emotional states to neutral expressions.

The deficits in identifying negative emotional states (anger, fear and sadness) have already been highlighted [40,41]. Unlike what emerged in many other studies, in our case the deficit is extended to the recognition of all emotions and not only to the negative ones.

In agreement with previous studies, our results show moreover that subjects with focal epilepsy were less able than their peers in Theory of Mind, that is the ability to perceive and correctly interpret other's mental states and behaviors, as well as to understand false beliefs, metaphors and irony [42].

Given the greater involvement of temporal regions in the genesis of social cognition abilities, and on the basis of previous studies, we have supposed a relationship between social cognition performance and lobe of origin of epilepsy [43]. However, in our sample the performances in social cognition (both in facial emotion recognition and in Theory of mind) seem not to be associated to other factors such as lobe and side of seizure onset. This result, in line with the new understanding of epilepsy as a “network disease”, could suggest that a shared underlying neural network may be affected in children with epilepsy, according to the hypothesis for which seizures arise from a diseased network, that involves overlapping cortical and subcortical structures, independently from a

Table 4
Performance in social cognition, executive function and cognitive abilities in children and adolescents in the epilepsy group and in the control group.M = mean; SD = standard deviation.

		EPILEPSY GROUP		Statistics
		Children	Adolescents	
		M ± S	M ± SD	
SOCIAL COGNITION				Student's t-test
Emotion recognition (ER)	standard score	5.83 ± 2.66	5.05 ± 2.68	t = 1.12, p = 0.267
(single emotions)				Mann-Whitney test
Neutral	error number	2.08 ± 2.06	1.58 ± 0.89	U = 444, p = 0.856
Happiness	error number	0.58 ± 0.97	0.37 ± 0.49	U = 444, p = 0.837
Sadness	error number	3.25 ± 1.51	3.32 ± 0.87	U = 434, p = 0.737
Fear	error number	1.33 ± 0.64	1.84 ± 1.24	U = 330, p = 0.054
Anger	error number	2.67 ± 1.69	2.05 ± 1.25	U = 366, p = 0.183
Disgust	error number	2.33 ± 1.05	1.84 ± 0.89	U = 330, p = 0.053
Theory of Mind (TM)	standard score	6.17 ± 2.20	6.53 ± 2.19	Student's t-test t = 0.63, p = 0.532
EPITRACK JUNIOR	standard score	27.17 ± 5.10	28.84 ± 3.53	Student's t-test t = 1.53, p = 0.132
RAVEN PROGRESSIVE MATRICES	standard score	88.83 ± 9.87	91.53 ± 7.73	Student's t-test t = 1.20, p = 0.235
		CONTROL GROUP		Statistics
		Children	Adolescents	
		M ± SD	M ± SD	
SOCIAL COGNITION				Student's t-test
Emotion recognition (ER)	standard score	5.35 ± 2.68	10.44 ± 1.00	t = 0.50, p = 0.623
				Mann-Whitney test
Neutral	error number	1.77 ± 1.46	0.84 ± 0.88	U = 50, p = 0.002
Happiness	error number	0.45 ± 0.72	0.16 ± 0.37	U = 122, p = 0.741
Sadness	error number	3.29 ± 1.15	1.44 ± 1.80	U = 50, p = 0.002
Fear	error number	1.65 ± 1.07	0.50 ± 0.67	U = 81, p = 0.040
Anger	error number	2.29 ± 1.45	1.13 ± 1.1	U = 62, p = 0.009
Disgust	error number	2.03 ± 0.97	1.67 ± 1.10	U = 117, p = 0.670
Theory of Mind (TM)	standard score	6.39 ± 2.18	9.69 ± 1.98	Student's t-test t = 0.40, p = 0.690
EPITRACK JUNIOR	standard score	28.19 ± 4.25	32.22 ± 2.92	Student's t-test t = 0.50, p = 0.618
RAVEN PROGRESSIVE MATRICES	standard score	90.48 ± 8.65	91.47 ± 10.44	Student's t-test t = 1.32, p = 0.198

M = mean; SD = standard deviation; p value <0.05 are in bold.

single pathological side [44].

On the other hand, the small sample size could have been a limit in identifying this difference, therefore this result should be confirmed through studies on larger sample.

A significant relationship between facial emotion recognition and ages of onset and duration of epilepsy was found. In particular subjects with lower performances have a long history of the disease. This data confirms what has already emerged from previous studies, and suggests that an early onset of epilepsy could interfere with the development of some neuronal networks important for social cognition [21,22,45].

Theory of Mind, instead, appears to be related to severity of epilepsy. In particular, children and adolescents who experience a high number of seizures show worse performance in this ability.

Different hypotheses can be advanced to explain this relationship: first of all, the seizures themselves could affect the neuronal network involved in social cognition abilities; on the other hand, a high number of seizures could affect executive functions, that consequently compromising social cognition; finally a greater severity of epilepsy could be associated with a social stigma, limiting the interactions with peers and reducing the opportunities for social experiences [46].

In accordance with previous studies [47], the executive functions are significantly compromised in patients with epilepsy compared to controls, unlike the non-verbal intelligence is preserved.

In the epileptic group, the social cognition performances are related to executive functions and non-verbal intelligence performances. In particular our results highlight that patients with greater impairment of executive functions and non-verbal intelligence, are also those who experience greater difficulty in recognizing facial expressions.

As already mentioned in the Introduction section, the relationship between cognitive abilities, executive functions and social cognition has been well established by several literature studies [26–32]. Our data confirms that this relationship could also be present in patients with epilepsy, on a par with what occurred in other neurological, psychiatric and neurodevelopmental conditions

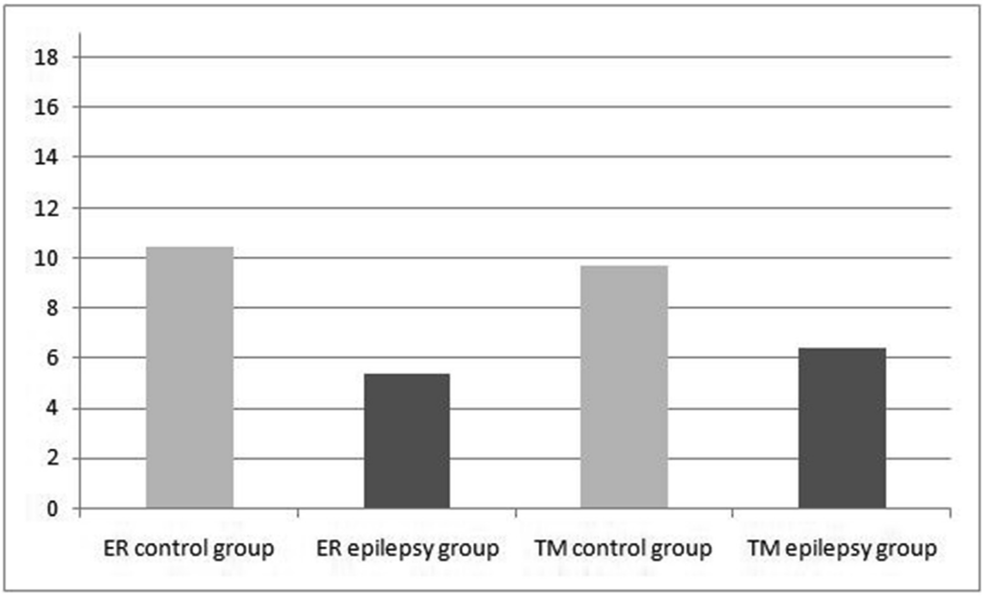

Fig. 1. Mean scores of Emotion Recognition and Theory of Mind in epilepsy group and in control group. ER = emotion recognition TM = Theory of Mind.

[48–50].

As already demonstrated in Attention Hyperactivity Deficit Disorder (ADHD) patients, the executive functions impairment can lead to a less focused attention in performing social cognition tasks; on the other hand, we can also assume that, in patients with epilepsy, there is a common mechanism that affects the maturation and development of different neuronal networks, involved in both, executive functions and social cognition abilities.

The comparison between children and adolescents in the epileptic group and in the control group highlighted some important information. In the epileptic group, children and adolescents did not differ significantly in terms of demographic and clinical features, except for the duration of epilepsy. Between the two subgroups there were no significant differences in the global score of ER, TM, RPM, EpiTrack Junior and also in the recognition of all the individual emotions.

In the control group there were no significant differences between children and adolescents in the global score of ER, TM, RPM, EpiTrack Junior and in the recognition of happiness and disgust; on the contrary there was a significant difference between the two subgroups in the recognition of fear, sadness and anger, in which younger children showed greater difficulties.

The results highlighted in the control group are in line with the developmental studies on the different trajectories of facial emotion perception. Happiness, which is typically the first recognizable emotion, depends on the amygdala and occipital lobes, that mature earlier in development [51]. Sadness, fear, anger and disgust, that are recognized later, rely on insula, pulvinar orbital frontal cortex and medial frontal gyrus, that progressively maturing from childhood to early adulthood [52].

In the epileptic group, on the other hand, this physiological, age-related difference in facial emotion perception has not been highlighted, and the deficits seem to be shared by both younger and older subjects. This result allows hypothesizing that epilepsy negatively affects the development and the maturation of neuronal networks involved in the facial emotion recognition.

The strength of our study is that it used an age-matched control group, and standardized direct neuropsychological tests. This study has also other limitations such as the modest sample size, the cross-sectional design and the fact that it doesn't consider the effect of anti-seizures drugs on the subjects' performances. As additional limit of the study, we specify that a correction for multiple comparisons has not carried out, because the statistical power would decreased and some significant differences in the analysis of the individual emotions would not have been highlighted.

A detailed evaluation of single emotions recognition should be performed in future investigations.

Another limitation of the study is the use of the EpiTrack Junior test, which, although it is a rapid and useful screening tool, provides a global score only and does not give information about the individual domains of the executive functions (e.g. attention, working memory, cognitive flexibility, inhibition control). It would be appropriate to conduct future studies with a more detailed assessment of executive function, in order to define better the neuropsychological profile of subjects with epilepsy and eventually correlate specific domains with social cognition performance.

In order to evaluate selective attention to detail and visuoperceptive abilities, it would be interesting to integrate the neuropsychological evaluation with specific tests such as the items "Completion of figures" of the WISC-IV battery.

There are numerous other future perspectives of investigation: social cognition could be evaluated in patients with different forms of epilepsy, both focal and generalized, and compare the results in order to highlight a possible common phenotypic profile associated with the different subgroups of patients. The effect of antiepileptic drugs could also be further evaluated. Furthermore, imaging studies could be added in order to correlate neuropsychological alterations to functional and structural neuroanatomical data. Prospective studies that assess social cognition over time would also be necessary to confirm and further investigate these results.

5. Conclusion

Our results suggest that children and adolescents with focal epilepsy had difficulties in facial emotion recognition and Theory of Mind, compared to their peer.

Both these difficulties seem to be independent of intelligence, but they could be related to some features of epilepsy itself. Our results also suggest that deficits in facial emotion recognition are potentially related to difficulties in executive functions, although it is not possible to establish a causal link between the two variables.

Since social skills such as the recognition of facial expressions and the Theory of Mind are basic aspects for the correct development of social relationships, these aspects should be monitored in the developmental age, in order to guarantee children and adolescents with epilepsy a good quality of life.

Declaration of competing interest

None of authors has any conflict of interest to disclose.

Acknowledgements

We thank all the participants who took part in this research, as well as their parents for the time spent during all evaluation.

References

[1] M. Lieberman, Social cognitive neuroscience: a review of core process, Annu. Rev. Psychol. 58 (2007) 259–289.
[2] R. Saxe, Uniquely human social cognition, Curr. Opin. Neurobiol. 16 (2) (2006) 235–239.
[3] I. Hasson-Ohayon, M. Mashiach-Eizenberg, N. Arnon-Ribenfeld, S. Kravetz, D. Roe, Neuro-cognition and social cognition elements of social functioning and social quality of life, Psychiatr. Res. 258 (2017) 538–543, https://doi.org/10.1016/j.psychres.2017.09.004.
[4] H.M. Genova, A. Genualdi, Y. Goverover, N.D. Chiaravalloti, C. Marino, J. Lengenfelder, An investigation of the impact of facial affect recognition impairments in moderate to severe TBI on fatigue, depression, and quality of life, Soc. Neurosci. 12 (3) (2017) 303–307, https://doi.org/10.1080/17470919.2016.1173584.
[5] F.M.C. Besag, M.J. Vasey, Social cognition and psychopathology in childhood and adolescence, Epilepsy Behav. 10 (18) (2019) 30881–30883, https://doi.org/10.1016/j.yebeh.2019.03.015, pii:S1525-5050.
[6] B. Şahin, K. Karabekiroğlu, A. Bozkurt, M.B. Usta, M. Aydın, ÇobanoğluC, The relationship of clinical symptoms with social cognition in children diagnosed with attention deficit hyperactivity disorder, specific learning disorder or autism Spectrum disorder, Psychiatry Investig 15 (12) (2018) 1144–1153, https://doi.org/10.30773/pi.2018.10.01.
[7] E. Stewart, S. Lah, M.L. Smith, Patterns of impaired social cognition in children and adolescents with epilepsy: the borders between different epilepsy phenotypes, Epilepsy Behav. 18 (2019) 106146, https://doi.org/10.1016/j.yebeh.2019.01.031.
[8] C.D. Frith, U. Frith, Interacting minds – a biological basis, Science 286 (5445) (1999) 1692–1695.
[9] J.R. Conway, G. Bird, Conceptualizing degrees of theory of mind, Proc. Natl. Acad. Sci. U. S. A. 13 (7) (2018) 1408–1410, https://doi.org/10.1073/pnas.1722396115, 115.
[10] C.E. Izard, Innate and universal facial expressions: evidence from developmental and cross-cultural research, Psychol. Bull. 115 (2) (1994) 288–299.
[11] C. Lenti, D. Lenti-Boero, A. Giacobbe, Decoding of emotional expressions in children and adolescents, Percept. Mot. Skills 89 (3 Pt 1) (1999) 808–814.
[12] R. Adolphs, Neural systems for recognizing emotion, Curr. Opin. Neurobiol. 12 (2002) 169–177.
[13] M. Batty, M.J. Taylor, The development of emotional face processing during childhood, Dev. Sci. 9 (2) (2006) 207–220.
[14] E.E. Nelson, E.B. McClure, C.S. Monk, E. Zarahn, E. Leibenluft, D.S. Pine, et al., Developmental differences in neuronal engagement during implicit encoding of emotional faces: an event-related fMRI study, JCPP (J. Child Psychol. Psychiatry) 44 (7) (2003) 1015–1024.
[15] E.J. Kilford, E. Garrett, S.J. Blakemore, The development of social cognition in adolescence: an integrated perspective, Neurosci. Biobehav. Rev. 70 (2016) 106–120, https://doi.org/10.1016/j.neubiorev.2016.08.016.
[16] B.A. Völlm, A.N. Taylor, P. Richardson, R. Corcoran, J. Stirling, S. McKie, et al., Neuronal correlates of theory of mind and empathy: a functional magnetic resonance imaging study in a nonverbal task, Neuroimage 29 (1) (2006) 90–98.
[17] C.E. Mathy, L.J. Moses, J.H. Pfeifer, How and where: theory-of-mind in the brain, Dev Cogn Neurosci 7 (2006) 268–277.
[18] H. Jokeit, M. Eicher, V. Ives-Deliperi, Towards social neuropsychology of epilepsy: a review on social cognition in epilepsy, Acta Epileptologica 1 (2019) 8–17, https://doi.org/10.12107/ae.2018.1.3.
[19] P. Fusar-Poli, A. Placentino, F. Carletti, P. Landi, P. Allen, S. Surguladze, et al., Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies, J. Psychiatry Neurosci. 34 (2009) 418–432.
[20] V.L. Ives-Deliperi, H. Jokeit, Impaired social cognition in epilepsy: a review of what we have learnt from neuroimaging studies, Front. Neurol. 10 (2019) 940, https://doi.org/10.3389/fneur.2019.00940.
[21] S. Meletti, F. Benuzzi, G. Rubboli, G. Cantalupo, M. Stanzani Maserati, P. Nichelli, et al., Impaired facial emotion recognition in early-onset right mesial temporal lobe epilepsy, Neurology 11 (60) (2003) 426–431.
[22] S. Meletti, F. Benuzzi, G. Cantalupo, G. Rubboli, C.A. Tassinari, P. Nichelli, Facial emotion recognition impairment in chronic temporal lobe epilepsy, Epilepsia 50 (6) (2009) 1547–1559, https://doi.org/10.1111/j.1528-1167.2008.01978.x.
[23] E. Stewart, C. Catroppa, D. Gill, R. Webster, J. Lawson, A. Mandalis, et al., Theory of Mind and social competence in children and adolescents with genetic generalised epilepsy (GGE): relationships to epilepsy severity and anti-epileptic drugs, Seizure 60 (2018) 96–104, https://doi.org/10.1016/j.seizure.2018.06.015.
[24] E. Stewart, C. Catroppa, S. Lah, Theory of mind in patients with epilepsy: a systematic review and meta-analysis, Neuropsychol. Rev. 26 (1) (2016) 3–24, https://doi.org/10.1007/s11065-015-9313-x.
[25] A. Diamond, Executive functions, Annu. Rev. Psychol. 64 (2013) 135–168, https://doi.org/10.1146/annurev-psych-113011-143750.
[26] M. Wade, H. Prime, J.M. Jenkins, K.O. Yeates, T. Williams, K. Lee, On the relation between theory of mind and executive functioning: a developmental cognitive neuroscience perspective, Psychon. Bull. Rev. 25 (6) (2018) 2119–2140, https://doi.org/10.3758/s13423-018-1459-0.
[27] R.T. Devine, N. White, R. Ensor, C. Hughes, Theory of mind in middle childhood: longitudinal associations with executive function and social competence, Dev. Psychol. 52 (5) (2016) 758–771, https://doi.org/10.1037/dev0000105.
[28] T. Zhang, L. Chen, Y. Wang, M. Zhang, L. Wang, X. Xu, et al., Impaired theory of mind in Chinese children and adolescents with idiopathic generalized epilepsy: association with behavioral manifestations of executive dysfunction, Epilepsy Behav. 79 (2018) 205–212, https://doi.org/10.1016/j.yebeh.2017.12.006.
[29] M. Dricu, S. Frühholz, Perceiving emotional expressions in others: activation likelihood estimation meta-analyses of explicit evaluation, passive perception and incidental perception of emotions, Neurosci. Biobehav. Rev. 71 (2016) 810–828.
[30] T. Liu, T. Xiao, X. Li, J. Shi, Fluid intelligence and automatic neural processes in facial expression perception: an event-related potential study, PloS One 16 (9) (2015), e0138199, https://doi.org/10.1371/journal.pone.0138199, 10.
[31] K. Schlegel, J.S. Witmer, RammsayerTH, Intelligence and sensory sensitivity as predictors of emotion recognition ability, J. Intell. 8 (4) (2017) 5, https://doi.org/10.3390/jintelligence5040035.
[32] K. Schlegel, T. Palese, M.S. Mast, T.H. Rammsayer, J.A. Hall, N.A. Murphy, A meta-analysis of the relationship between emotion recognition ability and intelligence, Cognit. Emot. 34 (2) (2020) 329–351, https://doi.org/10.1080/02699931.2019.1632801.
[33] C. Urgesi, F. Campanella, F. Fabbro, NEPSY-II Italian Version, Giunti OS, Firenze, Italy, 2011.
[34] T. Zilli, S. Zanini, S. Conte, R. Borgatti, C. Urgesi, Neuropsychological assessment of children with epilepsy and average intelligence using NEPSY II, J. Clin. Exp. Neuropsychol. 37 (10) (2015) 1036–1051, https://doi.org/10.1080/13803395.2015.1076380.
[35] C. Helmstaedter, K. Schoof, T. Rossmann, G. Reuner, A. Karlmeier, G. Kurlemann, Introduction and first validation of EpiTrack Junior, a screening tool for the assessment of cognitive side effects of antiepileptic medication on attention and executive functions in children and adolescents with epilepsy, Epilepsy Behav. 19 (1) (2010) 55–64, https://doi.org/10.1016/j.yebeh.2010.06.042.
[36] N.E. Kadish, M. Baumann, J. Pietz, S. Schubert-Bast, G. Reuner, Validation of a screening tool for attention and executive functions (EpiTrack Junior) in children and adolescents with absence epilepsy, Epilepsy Behav. 29 (1) (2013) 96–102, https://doi.org/10.1016/j.yebeh.2013.06.004.
[37] J. Raven, J.C. Raven, J.H. Court, Manual for Raven's Progressive Matrices and Vocabulary Scales, Harcourt Assessment, San Antonio, TX, 2003 updated 2004.
[38] L. Picone, A. Orsini, L. Pezzuti, Le Matrici Progressive di Raven: contributo alla taratura italiana per soggetti tra i 6 e i 18 anni, Giunti Psychometrics S.r.l. – Firenze (2018).
[39] M. Edwards, E. Stewart, R. Palermo, S. Lah, Facial emotion perception in patients with epilepsy: a systematic review with meta-analysis, Neurosci. Biobehav. Rev. 83 (2017) 212–225, https://doi.org/10.1016/j.neubiorev.2017.10.013.
[40] N. Golouboff, N. Fiori, O. Delalande, M. Fohlen, G. Dellatolas, Jambaquél, Impaired facial expression recognition in children with temporal lobe epilepsy: impact of early seizure onset on fear recognition, Neuropsychologia 46 (5) (2008) 1415–1428.
[41] K.A. Bujarski, L. Flashman, Z. Li, T.D. Tosteson, B.C. Jobst, V.M. Thadani, et al., Investigating social cognition in epilepsy using a naturalistic task, Epilepsia 57 (9) (2016) 1515–1520, https://doi.org/10.1111/epi.13477.
[42] N. Morou, V. Papaliagkas, E. Markouli, M. Karagianni, E. Nazlidou, M. Spilioti, et al., Theory of Mind impairment in focal versus generalized epilepsy, Epilepsy Behav. 88 (2018) 244–250, https://doi.org/10.1016/j.yebeh.2018.09.026.
[43] Bora E, Meletti S. Social cognition in temporal lobe epilepsy: a systematic review and meta-analysis. Epilepsy Behav.;60:50-57. Doi:10.1016/j.yebeh.2016.04.024.
[44] D.J. Englot, P.E. Konrad, V.L. Morgan, Regional and global connectivity disturbances in focal epilepsy, related neurocognitive sequelae, and potential mechanistic underpinnings, Epilepsia 57 (10) (2016) 1546–1557, https://

doi.org/10.1111/epi.13510.
[45] U. Hlobil, C. Rathore, A. Alexander, S. Sarma, K. Radhakrishnan, Impaired facial emotion recognition in patients with mesial temporal lobe epilepsy associated with hippocampal sclerosis (MTLE-HS): side and age at onset matters, Epilepsy Res. 80 (2–3) (2008) 150–157, https://doi.org/10.1016/j.eplepsyres.2008.03.018.
[46] A. Jacoby, J.K. Austin, Social stigma for adults and children with epilepsy, Epilepsia 48 (Suppl 9) (2007) 6–9.
[47] W.S. MacAllister, M. Vasserman, J. Rosenthal, E. Sherman, Attention and executive functions in children with : what, why, and what to do, Appl Neuropsychol Child 3 (3) (2014) 215–225, https://doi.org/10.1080/21622965.2013.839605.
[48] M. Guida, L. Caciagli, M. Cosottini, U. Bonuccelli, F. Fornai, F.S. Giorgi, Social cognition in idiopathic generalized epilepsies and potential neuroanatomical correlates, Epilepsy Behav. 100 (Pt B) (2019) 106118, https://doi.org/10.1016/j.yebeh.2019.01.003.
[49] M.M. Hurtado, M. Triviño, M. Arnedo, G. Roldán, P. Tudela, Are executive functions related to emotional intelligence? A correlational study in schizophrenia and borderline personality disorder, Psychiatr. Res. 246 (2016) 84–88, https://doi.org/10.1016/j.psychres.2016.09.027.
[50] A. Miranda, C. Berenguer, B. Roselló, I. Baixauli, C. Colomer, Social cognition in children with high-functioning autism Spectrum disorder and attention-deficit/hyperactivity disorder. Associations with executive functions, Front. Psychol. 8 (2017) 1035, https://doi.org/10.3389/fpsyg.2017.01035.
[51] C. Herba, M. Phillips, Annotation: development of facial expression recognition from childhood to adolescence: behavioral and neurological perspectives, JCPP (J. Child Psychol. Psychiatry) 45 (7) (2004) 1185–1198.
[52] L.A. Thomas, M.D. De Bellis, R. Graham, K.S. LaBar, Development of emotional facial recognition in late childhood and adolescence, Dev. Sci. 10 (5) (2007) 547–558.