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Frontal Lobe Epilepsies: Neuropsychological and Behavioral Consequences in Children

Chiara Vago, Sara Bulgheroni,
Silvana Franceschetti* and Daria Riva
*Developmental Neurology Division, and *Department of Neurophysiology and Epileptology, IRCCS Foundation Neurological National Institute C. Besta Italy*

1. Introduction

The frontal lobes of the brain constitute more than a third of the human cerebral cortex and are characterized by a complex functional organization supporting higher level integration circuits. Based on its cell architecture, the frontal lobe can be divided into two parts, the posterior and anterior, each with important functional characteristics. The posterior part controls motor activity and can be further divided into a premotor area that controls preparation for movement, and a motor area that governs the actual performance of movements. The anterior part, or prefrontal cortex, is fundamental to the processing of higher cognitive functions, such as planning, inhibitory control and capacity for judgment, and in mood control (Grossi & Trojano, 2007). Behind the complex functioning of the frontal lobe lie ample networks that involve cortical and subcortical structures. Diffusion tensor imaging studies have confirmed the presence of these multiple connections with age-related and gender-related changes (Pal et al., 2011).

The complexity of the frontal lobe, in terms of its neuroanatomy and connections, determines a marked variability in the epileptic manifestations with fast and inter- and intra-hemispheric propagation.

Generally speaking, focal epilepsies are often associated with neuropsychological, behavioral and emotional problems that can also affect a patient's adaptive functioning (Cornaggia et al., 2006). A frontal localization of the epileptic focus correlates with executive dysfunctions. The executive functions refer to higher-order, self-regulatory, cognitive processes that aid in the monitoring and control of thought and action. Numerous processes are associated with executive functions, the most important being anticipation, goal selection, planning, initiation of activity, self-regulation, mental flexibility, attentional control, metacognitve abilities such as error correction and detection, and the use of feedback. Executive skills are also implicated in motor planning, controlling impulses and regulating behavior (Lezak et al., 2004), as well as in emotional responses, behavioral and social actions. They consist of those capacities that enable a person to engage successfully in independent, purposeful, self-serving behavior (Gioia, et al. 2001).

Executive functions have been conceptualized as multiple process-related systems, that are inter-related, inter-dependent and function together as an integrated supervisory or control system (Lezak et al., 2004). Anderson (2002) proposed a model of executive functions

comprising four discrete but inter-related executive domains that work together to enable 'executive control'. These domains are: a) attentional control, which includes the capacity to selectively attend to specific stimuli and inhibit arrogant responses, the ability to focus attention for a prolonged period, the regulation and monitoring of actions; b) information processing, in terms of fluency, efficiency and speed of output; c) cognitive flexibility, i.e. the ability to shift between response sets, learn from mistakes and devise alternative strategies, divided attention and working memory; and d) goal setting domains, which include the ability to develop new initiatives and concepts, plan actions in advance and approach tasks in an efficient, strategic manner.

Executive skills emerge in the first year of life and develop rapidly throughout childhood: they begin to mature between 4 and 7 years of age, while the greatest changes occur between 8 and 12 years old, but the efficiency of an individual's executive abilities continues to increase between 12 and 15 years old and even in adulthood. The different functions in the executive domains develop at different rates. For example, attentional control appears to emerge in infancy and develops rapidly in early childhood. In contrast, cognitive flexibility, goal setting and information processing have a sensitive period between 7 and 9 years of age, and are relatively mature by the time a child is 12. A transitional period is thought to coincide with the start of adolescence, and executive control would emerge soon afterwards (Hughes et al., 2010). The frontal lobes mature progressively at neuroanatomical level too, the result of a combination of myelogenesis (Klingberg et al., 1999) and synaptogenesis (Huttenlocher & Dabholkar, 1997) interacting with the environment.

This chapter concentrates on nonlesional epilepsies involving the frontal lobe: first, we briefly describe the characteristic EEG discharges; then we concentrate on the neuropsychological and behavioral consequences, in the light of the complexity of frontal regions; finally, we pay attention to the interactions between EEG features, demographic variables and neuropsychological outcome.

2. Frontal lobe epilepsy

2.1 Characteristics of EEG discharges

Frontal lobe epilepsy (FLE) is the second most common type of focal epilepsy, accounting for 20-30% of cases. It is also the second most frequent reason for the surgical treatment of epilepsy, affecting approximately 20% of patients with refractory focal epilepsy (Lee et al., 2008). The EEG trace shows partial frontal anomalies frequently with a secondary generalization and a rapid and diffuse propagation of the epileptic activity to the contralateral hemisphere. The seizures deriving from this type of anomaly are usually brief, rich in motor signs, and often occur at night, though their precise features depend on the lateralization and specific site of the epileptic focus (Patrikelis et al., 2009). Usually, a focus in the primary motor cortex prompts focal motor seizures, while foci in the supplementary motor area give rise to tonic seizures, and involvement of the orbital, medial and dorsolateral regions induces complex partial seizures.

2.2 Neuropsychological functioning

The number of works on adult subjects has increased in recent years. Adults with FLE generally have an intelligence within the normal range and deficits in response inhibition and impulse control, attention, motor programming and speed (for a review see Patrikelis et al., 2009). Fewer studies have been performed on patients of developmental age. FLE

children share many of the features of frontal lobe dysfunctions in adult patients, but the differences in the neuropsychological tests used and, more importantly, the late development of the frontal lobe and the functions it serves mean that findings in adults cannot be extended to patients of developmental age.

Most studies on children with FLE reported cognitive capacities in the normal range (Culhane-Shelburne et al., 2002; Hernandez et al., 2002, 2003; Luton et al., 2010; Riva et al., 2002, 2005), whatever the features of their seizures. Prevost et al. (2006), on the other hand, conducted a retrospective study on 21 children with FLE with a mean age of 6 years (though the age range was very wide, from less than 1 to more than 13 years of age), and found that only 52% had a normal IQ, as measured with the Wechsler scales (WPPSI-R and WISC-III); more detailed results are not provided, however.

In actual fact, the majority of the studies on FLE children investigate the efficiency of their executive functions comparing them to children with temporal lobe epilepsy (TLE) and generalized epilepsy with absences (GEA) besides to children tipically development.

Hernandez et al. (2002) compared 16 children who had frontal lobe epilepsy with 8 cases of TLE and 8 of GEA, all between 8 and 16 years old; they used a broad neuropsychological test battery to determine whether children with FLE had deficits in only some or all of the components of executive skills. The FLE children showed deficits in planning ability, as assessed by the Tower of London (TOL) test, in which children are asked to copy a modeled pattern of three colored beads in a prescribed number of trials, planning and anticipating their actions. The FLE children's initial planning times were shorter, but their total performance times were longer: they both made their first move immediately after the model was placed before them, and they ignored the instruction to move one bead at a time, but they took longer to complete the models than the children with TLE or GEA, and the healthy control group. No significant differences were seen between the groups for the number of models completed in the first trial or the total number of trials needed to correctly reproduce the model proposed by the examiner (variables that reflect the subject's planning ability). These findings globally indicate that these children's poor planning ability is due mainly to a tendency to act impulsively: they tended to start working on the task promptly but inaccurately, subsequently slowing down and taking a long time to complete the process. The authors also reported deficits in the Verbal Fluency Test, in which children are asked to a produce as many different words as possible according to a given letter (phonemic condition) or category (semantic condition) within one minute. The majority of FLE children has considerable difficulty generating words in the phonemic condition. There may also be a reduced output in the semantic condition, however, as recently confirmed by Luton et al. (2010) in 20 children with FLE aged between 8 and 19 years. In quality terms, there are reports of an initially very long latency (with children taking 20 seconds or more to produce their first word) and continuous hesitations throughout the test. Riva et al. (2005) also found a limited efficiency in terms of verbal fluency, with significantly lower results for phonemic fluency, while semantic fluency was within normal range in 17 FLE children 6-14 years of age. A limited output was recorded in a design fluency task too, with a significantly higher number of perseverative than non-perseverative errors (Riva et al., 2002, 2005). The test involved the child first having to draw as many different abstract shapes as possible (free form); then, in the second part of the test, a set number of lines was specified for each shape (fixed form). Perseverations (i.e. repetitions of designs) are considered a problem typical of patients with frontal lesions, and especially those involving the prefrontal cortex.

The difficulties in verbal and design fluency tasks would seem to that FLE children have greater difficulty both in mobilizing their resources to initiate a verbal and non-verbal search, and in being flexible in their search strategy in compliance with certain rules.
In a later work, Hernandez et al. (2003) looked at sustained attention and inhibition control using visual and auditory tasks. FLE children had a significantly lower Perceptual Speed Index in the WISC-III, scoring lower in both the Symbol Search and the Coding subtests (although the difference was only statistically significant for the former) by comparison with GEA children, but not with TLE children. It is important to emphasize that the results for FLE children fell in the borderline range vis-à-vis normative scores, while the other clinical groups had scores within the average range. Qualitative analyses showed that FLE children were not only slower, but they also made more mistakes than the other groups. In addition to these two tests with visual stimuli, an auditory version of the Continuous Performance Test (CPT) was administered, in which children had to respond only to the letter A, to assess sustained attention and inhibitory control. FLE children were impaired more than TLE children, but not more than GEA children. All three groups omitted some targets, but FLE children produced significantly more false-positive responses. Here again, this finding suggests an impulsive response mode and a weaker capacity to inhibit irrelevant, but highly activated response patterns. Children with FLE fared poorly also in a second conditions of the CPT, in which a target letter changes following an alphabetical sequence posing considerable demands on working memory. They obtained fewer correct responses than the other two groups because they lost the sequence much earlier in the course of the task: the majority of children with FLE (63%) did not produce more than four correct responses before losing track of the sequence.
Culhane-Shelburne et al. (2002) also studied attention abilities, inhibitory control and flexibility of response, comparing 12 FLE children with 15 TLE children between 8 and 18 years of age. In spite of there was a marked variability within both groups, the results confirm the FLE children's difficulties in the sphere of attention and control over highly activated responses, but not the specificity of this deficit respect to TLE children. In the Test of Variables of Attention (TOVA), a computerized fixed visual continuous performance task, the mean scores for both inattention (errors of omission) and impulsivity (errors of commission) fell below 2 standard deviations from the norm, with no significant differences emerging between FLE and TLE children while in the Stroop Color Word Test onley the FLE children made more mistakes.
Auclair et al. (2005) compared the performance of a sustained attention task in 18 FLE children, 10 children with TLE and 9 controls, aged 8 - 16 years. The task they used was developed starting from LaBerge's theory of attention (1997), which distinguishes between three aspects of attention, i.e. selection, preparation and maintenance. The children had to respond to a target presented in the center of a display and ignore a distracter appearing to the right or left of the target. The distracter was presented before the target and the relative frequency of presentation of the distracter and target varied within a set of trials (0%, 33%, 67%). This task requires a high level of attention control, and should therefore strongly involve executive control, which requires planning, decision-making and self-regulation related to attention control. The authors reported a deficit in preparatory attention in FLE children by comparison with both controls and cases of TLE. Preparatory attention is prolonged and focuses on a particular forthcoming target, often in the presence of distracting stimuli (LaBerge, 1997). This aspect of attention is largely influenced by the expectation that a given event will occur and enables a faster and more efficient response to

competing stimuli. FLE children reacted more slowly to a target stimulus as a function of how often the distractors appeared during the test, i.e. the higher the likelihood of a distractor appearing, the longer the time it took them to react to the target stimulus. This indicates that FLE children have an impaired sensitivity to the chances of a distractor appearing and are consequently less able to resist this interference, suggesting that impairments involving frontal regions reduce the individual's ability to prepare to focus their attention on the upcoming target.

Deficits in attention skills are consistent with clinical observations in children with frontal lobe injuries of different aetiology, such as tumour, stoke, cerebral marfomations, trauma (Jacobs et al., 2007), and also with imaging studies showing a reduced activation in the frontal cortex in patients with attention deficit disorder (Helpern et al., 2011).

Another important function of the executive domain is cognitive flexibility. In FLE children, there are clinical descriptions of rigid, inflexible behavior, difficulty changing activity or procedure, failure to adapt to new or unusual demands. Neuropsychological laboratory measures are not sensitive enough to identify mental flexibility problems, however. To the best of our knowledge, only Igarashi et al. (2002) found deficient results in the Wisconsin Card Sorting Test (WCST) in 15 FLE children 8-20 years of age. The mean results indicated a lower number of matching criteria and a higher number of perseverative errors by comparison with 19 children with TLE, with and without structural lesions, and 30 controls. Riva et al (2002) reported an impaired performance with more perseverative responses and numerous non-perseverative errors, but these results were not confirmed in a subsequent study on a larger sample (Riva et al., 2005). Hernandez et al. (2002) found no differences in performance using the WCST when FLE and TLE children were compared with cases of GEA, although the FLE children tended to perform qualitatively more impulsively (e.g. placing the card quickly without paying attention to the feedback), or they had greater difficulties in following instructions (e.g. taking any card from the pile in spite of being repeatedly told to always take the first card). When the results were compared with normative scores, all the children with epilepsy completed an adequate number of categories, but the FLE children seemed to produce more perseverative responses and perseverative errors. A possible explanation for this lies in that the WCST is a multifactorial task that involves functions that are not all mediated by the frontal lobe (Sanchez-Carpintero & Neville, 2003) as confirmed by lesional studies that found no differences between patients with and without frontal lesions (Nyhus & Barcelò, 2009).

Working memory and strategic memory skills are also affected in patients with frontal epilepsy. Several studies have used the California Verbal Learning Test, which involves learning a list of semantically correlated words and then investigating its recall after presenting an interfering list (immediate recall), and again after a 20 minute interval (delayed recall). FLE children have a normal capacity for immediate and delayed recall (Culhane-Shelburne et al., 2002; Hernandez et al., 2003; Riva et al., 2002) but learning slope showed that the FLE children tended to decline in the last of the five trials, while children with temporal or generalized epilepsy showed a marked increase in the number of items they recalled. This difference was not statistically significant, but suggests a limited capacity of FLE children to sustain adequate attentional levels over time. No significant differences emerged concerning the number of perseverations or semantic clusters during the five learning trials, or in the immediate and delayed recall of the first list (Hernandez et al., 2003; Riva et al., 2005), whereas there was evidence of a significantly higher number of intrusions

and a weaker capacity to resist retroactive and proactive interferences (Hernandez et al., 2003).

Tasks that entailed copying and recalling visual material confirmed that FLE children have a poor visuo-perceptive organization and a greater impulsiveness in completing the copy, which led to a lower accuracy when it came to recalling the stimulus. In the Rey Complex Figure Test, FLE children scored lower than TLE and GEA children for copying the figure and also for immediate recall (Hernandez et al., 2003). The role of the frontal lobes in the memory process can be defined as strategic, i.e. the frontal lobes exercise control over memory by coordinating, elaborating and interpreting the associations taking place in the medial temporal lobe (Stuss & Levine, 2002). Neuroimaging studies with fMRI (Prince et al., 2005; Wagner et al., 2001) provide evidence of the activation of frontal brain areas associated with the organization of material during encoding. The frontal lobe also has a role in compiling retrieved material into an episodic representation, and monitoring the relevance of retrieved information according to a task-related goal (Cabeza et al., 2003; Fletcher et al., 1996).

Few studies have investigated language skills: Cohen and Le Normand (1998) conducted yearly evaluations of receptive and expressive language skills in a sample of 6 children with left frontal seizures, comparing the results with a control group. Analyses of individual language trajectories revealed a clear dissociation in linguistic performance between comprehension and production. Linguistic comprehension gradually improved, reaching normal performance levels by the age of 7, while production remained rather poor even later on. Vannasse et al. (2005) found that school-aged children with FLE had significant deficits in phonological processing tasks when compared with children with TLE and GEA; more specifically, FLE subjects fared poorly on more elaborate or cognitively demanding metaphonological tasks. These findings suggest that an epileptic dysfunction originating from the frontal lobes hinders the more elaborate acquisitions involved in phonological development. These results are consistent with previous findings from neuroimaging studies on dyslexic individuals, which revealed activation anomalies in the frontal lobes (Pugh et al., 1996).

Finally, taking a look at fine unimanual and bimanual coordination and the planning and execution of sequences of single motor actions, there are reports of FLE children being slow and having a reduced manual dexterity, with sluggish and stiff or, conversely, over-hasty movements (Hernandez et al., 2002; Riva et al., 2002, 2005). They appear to find it difficult to maintain a fluid sequence of movements and tend to use spatial or verbal strategies to orient their movements, particularly during the performance of Luria's Motor Sequences task, which involves mutual and asymmetrical gestures with both hands, in which FLE children make far more mistakes in the motor sequence, rarely getting the sequences completely right, with a greater impairment in the intermanual tests and when using the non-dominant hand - a finding interpreted as relating to this hand being less well trained and consequently less able to perform new motor tasks. This would seem to indicate that frontal lobe epilepsy interferes with the more complex aspects of motor activity, which involve both the hemispheres (Hernandez et al., 2002).

2.3 Behavioral features

Frontal anomalies not only affect the higher cognitive functions, they also cause emotional and behavioral problems (Prevost et al. 2006); in this setting, data come both from direct clinical observation and from questionnaires completed by parents, who generally report

irritability, hyperactivity, impulsiveness, hyperkinesia and mood changes (Parisi et al., 2010).

Using the Child Behavior Checklist (CBCL), FLE patients have returned higher scores than TLE children on the Attention problem scale, and than GEA children on the Thought problem scale. Attention problems reported by the parents of children with FLE include absentmindedness, confusion, daydreaming, nervousness, anxiety, impulsiveness, difficulty in maintaining their concentration and in remaining seated. Irritability and concentration difficulties are frequently reported by parents of TLE children too, while absentmindedness and social immaturity are more often reported for cases of GEA. It is only for FLE children, however, that attentional problems fall within the clinical range. The thought problems frequently described in FLE children were recurring ideas and repetitive behavior. Also in the Competence scales of the CBCL parents report FLE children tending to be less socially active than other children with epilepsy: they rarely join groups or associations, the quality and quantity of their friendly relations are inferior, and their school performance is worse, although no significant differences emerge. These findings could be due to the questionnaire being designed mainly to investigate the children's emotional-behavioral functioning, while the Competence Scale is less sensitive. Parents have also reported having lower expectations concerning their epileptic children's academic performance (whatever the type of epilepsy involved), and their chances of becoming independent and being successful in life, by comparison with their other non-epileptic sonsA retrospective study reported cognitive and behavioral difficulties in a small sample of school-aged FLE children: the majority had an attention deficit disorder with hyperactivity or impulsiveness (14 of 21 children) and other behavioral problems (8 of 21); 60% (6 of 10) had learning difficulties requiring special support teaching. Almost all children whose seizures had begun before 6 years of age developed a learning disability. Their poor school performance seems to have numerous causes, involving behavioral more than cognitive problems (Prevost et al., 2006). It may be that children react to the constant negative feedback from the environment and such lower expectations may prevent children from reaching their full potential, accentuating their difficulties (Hernandez et al., 2003).

A review of qualitative data suggests that behavioral and academic problems are common in children with epileptic anomalies, but the Behavior Rating Profile-Second Edition (BRP-2) has not proved sensitive enough to detect the particular problems shown in FLE children (Culhane-Shelburne et al., 2002). Luton et al. (2010) used the Behavior Rating Inventory of Executive Function and confirmed that FLE children have a limited capacity for self-regulation and independent organization, they are easily distracted, and they have difficulty in completing a task assigned to them and in assessing their own progress as they go along.

The cognitive and behavioral problems of children with focal epilepsies often also interfere with the development of adaptive and social skills (Cornaggia, 2006). This was confirmed by Culhane-Shelburne et al. (2002), who reported a poor adaptive functioning, as assessed using the Vineland Adaptive Behavior Scales (VABS), in which FLE children obtain slightly lower than normal scores in all three subdomains: Communication, Daily abilities and Socialization. A two-step regression procedure showed that some of the measures of executive functioning have a strong bivariate relationship with the total score on the VABS. This would seem to confirm that executive functions are a crucial component not only of cognitive development, but also of adaptation to life in developmental age.

2.4 Relationship between neuropsychological data and clinical features

In dealing with the relationship between neuropsychological data and clinical variables, it is important first of all to consider that the majority of studies contain speculations on the qualitative analysis of the data without using statistical analyses. It is generally agreed that the impairment of a patient's neuropsychological function is greater, the earlier the age of onset of their epileptic seizures, particularly as concerns the executive functions, which have a lengthy developmental trend and functional improvements can occur into adult age (Hernandez et al., 2002, 2003; Prevost et al., 2006, Riva et al., 2002, 2005; Upton & Thompson, 1997). Cognitive evaluation and clinical follow-up should therefore be particularly accurate in patients with early-onset epilepsy.

Some works compared younger children (8-12 years) with older children (13-16 years), finding that the children under 12 had a worse outcome for verbal search, working memory, sustained attention, verbal and visual memory and behavioral problems. Comparisons between younger and older children with FLE also showed that the younger children did less well in uni- and bimanual tasks for the non-preferred hand, in the alternate tapping task for the preferred hand (Hernandez et al., 2002), in the working memory condition of the CPT, and in the copy and immediate recall on the Rey Complex Figure Test (Hernandez et al., 2003).

There are few and controversial data relating to the correlation between the frequency of seizures and neuropsychological findings: one study by Riva et al. (2002) reported a significant correlation with the Picture Completion Test of the WISC-R, which was not confirmed in the subsequent study (Riva et al., 2005).

No studies have found different types of cognitive function based on the side of the epileptic focus and its uni- or bilaterality. The often troublesome differentiation between left and right frontal dysfunctions in FLE may be attributable to the widespread, bilateral, rapid propagation of frontal seizures, which may make lateralized differences in cognitive measures difficult to distinguish. Unfortunately it is impossible to divide patients according to the exact location of their epileptic focus on the basis of EEG findings obtained with surface recordings and clinical ictal features. This problem can be addressed by means of thorough neuropsychological tests on different frontal functions in patients with FLE undergoing presurgical invasive deep-electrode EEG recordings, correlating their cognitive profiles with the seizure lateralization identified (Patrikelis et al., 2009).

3. Benign epilepsy of childhood with centrotemporal spikes

3.1 Characteristics of EEG discharges

Benign epilepsy with centrotemporal spikes (BECTS) or rolandic epilepsy is the most frequent form of epilepsy in school-aged children, accounting for 15%-25% of all childhood epilepsy. Seizures commonly occur during sleep, often in the early morning hours, with focal paresthesias and tonic or clonic arm or facial contractions, and may subsequently become generalized. Daytime seizures may occasionally occur, however. The conditions develops between 3 and 13 years old, with a male predominance. In most patients, rolandic discharges are detected over the centrotemporal brain regions, but other regions can also be involved. The location of the interictal epileptic activity may vary, but prominently involves the temporal or rolandic regions; moreover, spikes are often multifocal with a bilateral and asynchronous presentation, and they can even show an ipsilateral location with respect to the side of the body affected by the ictal phenomena. It is important to perform a wake-sleep

EEG recording because the spike-wave discharges are activated as the patient enters the sleep phase (Shields & Snead, 2009). BECTS carries a good prognosis irrespective of any intake of antiepileptic medication, with a normalization of the EEG trace and spontaneous remission of the seizures before puberty (Stephani & Carlsonn, 2006). In a meta-analysis of studies conducted on BECTS, Bouma et al. (1997) found that 50% of patients have a normalization of the EEG by the time they are six years old, 92% by 12 years old, and there is a near 100% remission by 18 years of age. Early studies suggested an autosomal dominant inheritance, based on EEG findings in siblings (Degen & Degen, 1990; Heijbel et al., 1975), while later studies suggested a multifactorial inheritance (Doose et al., 1997; Neubauer et al., 2000). More recently, Vadlamudi (2006) conducted a multicentre study on 18 pairs of twins, and claimed that the genetic factor is less important than was initially assumed, since the study demonstrated no concordant twin pairs with classic BECTS.

3.2 Neuropsychological and behavioral profile

Numerous studies have now been performed on the neuropsychological outcome in children with BECTS. A recent literature review reported that children with BECTS are at risk of mild cognitive impairment, though the prognosis for seizure outcome is excellent (Nicolai et al., 2006). The majority of the studies report normal intellectual abilities (Northcott et al., 2005; Riva et al., 2007; Volkl-Kernstock et al, 2006). Weglage et al. (1997) and Northcott et al. (2007) recorded lower results for IQs measured with the Wechsler Scales than in controls, but the scores were within the average range for the BECTS children too. As for neuropsychological function, the recent literature reports a wide spectrum of deficits, but no uniform definition of a specific neurocognitive profile has been established as yet. The subtle dysfunctions described were only apparent on intensive neuropsychological testing at a single time in the course of epilepsy and they caused no difficulties in real life (Massa et al., 2001).

Numerous studies found deficits in speech-related abilities. Staden et al. (1998) prospectively studied 20 children, selected irrespective of any history of learning or language problems. Thirteen children (65%) showed language difficulties in 2 or more of 12 language tests, and 8 children (40%) had specific language impairments. Other works reported worse results in tasks involving expressive (Baglietto et al, 2001; Volkl-Kernstock et al, 2009) and receptive vocabulary (Danielsson and Petermann, 2009; Volkl-Kernstock et al, 2009), and in phonological awareness (Northcott et al, 2005). We studied cognitive functions and language abilities in the group of 24 children with BECTS who were compared with a group of 16 age-matched controls. In BECTS we found preserved naming skills but lower results phonemic fluency, verbal re-elaboration of semantic knowledge, and lexical comprehension (Riva et al., 2007). The review of Overliet et al. (2010) concluded that language is often affected in children with centrotemporal anomalies, although the type of impairment reported varies in different studies. More recently the same authors (Overliet et al., 2011) reported a substantial percentage of their clinical sample of 48 children with BECTS (17-21%) receiving speech therapy before the onset of epilepsy. It remains to be seen whether the language impairment develops gradually after the onset of the epileptic anomalies, or whether rolandic epilepsy and language impairment are both symptoms of an underlying syndrome, or both develop during the process of epileptogenesis, as observed in some children whose language impairment developed before the onset of epilepsy.

Another interesting area of research concerns the effects of rolandic spikes on functional lateralization of language. Already in 1988, Piccirilli et al. investigated language

organization in 22 right-handed BECTS children, 14 of them with a left-sided and 8 with a right-sided electroencephalographic focus. The children were asked to perform two tasks simultaneously, i.e. a verbal task (they were asked to repeat the names of four animals) combined with right- or left-hand finger tapping. The verbal task interfered more with right-hand than with left-hand tapping rates in children with a right-sided electroencephalographic focus and in healthy controls, while in children with a left-sided electroencephalographic focus, the verbal task equally affected left-hand and right-hand performance. The authors concluded that epileptiform activity in BECTS may modify language lateralization, suggesting a bihemispheric representation. Hommet et al. (2001) obtained similar results in 23 adolescents and young adults in complete remission of BECTS, suggesting the persistence of a long-term hemispheric language representation disorder. Although the results were not statistically significant, qualitative analysis of the dual-task procedure in a sub-group of right-handed BECTS patients showed that those in remission after an initial right seizure demonstrated the same pattern as controls, whereas BECTS patients with an initial left focus showed an inverse pattern, with a right percentage change (i.e. the functional reduction affecting the right hand due to the interference of the verbal task) lower than the left percentage change in 5 of the 6 subjects. When the same group was assessed using the Dichotic Listening task (DL), the authors found no significant differences by comparison with the control group, but they attributed this result to a likely ceiling effect and consequently lower sensitivity of the test. Lundberg et al. (2005) found that 13 children with BECTS, whose side of focus was not specified, showed a right ear advantage but a significantly worse production of correct consonant-vowel syllables for left, right or both ears compared to controls. The authors interpreted this finding as an auditory discrimination deficit due to the proximity of the rolandic areas to the primary auditory receptive area. In 24 children with BECTS compared with 16 control subjects, our group found an atypical performance on DL with a loss of the usual advantage of the right ear/left hemisphere, associated with a functional right ear/left hemisphere advantage characteristic of controls in the same age range. This is not a case of a complete rightward shift, but of the loss of the advantage of one hemisphere over the other, suggesting that left hemispheric processing superiority for phonological stimuli is functionally disturbed by the interictal spikes, leading to a bi-hemispheric representation of the phonological processing of auditory, verbal stimuli (Bulgheroni et al., 2008).

More recently, fMRI was used to assess language lateralization in 20 children and 20 healthy controls. The fMRI analyses revealed that language-related activation was less lateralized to the left hemisphere in anterior brain regions in the BECTS children than in controls. This finding is consistent with the worse results in patients on the neuropsychological measures most dependent on the integrity of anterior aspects of language skills, such as naming and sentence production. So this study demonstrated that BECTS influences a language network that involves the more anterior, and therefore frontal cerebral regions (Lillywhite et al., 2009).

Difficulties have also been reported in academic perfomances (Nicolai et al., 2007) and learning, with deficits in reading (Ay et al., 2009; Fonseca et al., 2009; Papavasiliou et al, 2005; Piccirilli et al., 2008; Staden et al, 1998) and spelling (Monjauze et al, 2005; Papavasiliou et al, 2005; Staden et al, 1998).

Memory also seems to be negatively influenced by spikes in the centrotemporal area: there are reports of difficulties in short-term verbal memory (Danielsson & Petermann, 2009; Northcott et al, 2005; Weglage et al, 1997), visuo-spatial memory (Baglietto et al 2001;

Danielsson & Petermann, 2009; Volkl-Kernstock et al, 2009) and long-term verbal memory (Northcott et al, 2005) as well as in the learning of verbal information (Croona et al, 1999; Staden et al, 1998). We also investigated verbal learning and retrieval, and the use of learning strategies with the CVLT-C. The under 10-year-old patient showed significantly worse supraspan skills and were less efficient in using a semantic clustering strategy than their age-matched controls, while no such difference emerged for the over 10-year-olds. This suggests that the capacity for a spontaneous use of a more efficient strategy matures later in BECTS children (Vago et al., 2008).

All the above-mentioned works investigated functioning in school-aged BECTS children. Danielsson & Petermann (2009) found verbal and non-verbal difficulties relating to articulation, auditory and visual memory, language comprehension and visual-constructive performance, also in 25 BECTS children aged 4 – 7 years when compared with 25 healthy controls.

Finally, studies on executive functions in children with BECTS identified mild deficits in information processing (Baglietto et al, 2001; D'Alessandro et al, 1990), in inhibitory processes (Deltour et al., 2007, 2008), in problem solving (Croona et al, 1999), in cognitive flexibility (Croona et al, 1999; Deltour et al., 2007; Gunduz et al, 1999), and auditory attention (Ay et al., 2009). Recently Cerminara et al. (2010) used a computerized test battery to assess attention ability in 21 children with BECTS compared with 21 controls. They found an impairment in selectivity (impulsiveness, focused attention, selective attention, aspects of divided attention) and in one measure of intensity (arousal) of attention in children with rolandic epilepsy. Vigilance was not impaired in the clinical subjects.

An increased distractibility, impulsiveness and hyperactivity were often reported (Giordani et al, 2006; Massa et al, 2001; Metz-Lutz et al, 1999; Volkl-Kernstock et al., 2009). Holtmann et al. (2006) administered a neuropsychological battery focusing on attentional processing, cognitive efficiency, response inhibition, visuo-spatial and verbal short-term memory and language functions in 16 children with ADHD and BECTS, 16 with ADHD but no EEG discharges, and 16 healthy controls. The first clinical group performed worse than the other two in a variety of CPT and Stroop test measures. In particular, they made significantly more commission errors, reflecting impaired inhibition of an ongoing response. They also had pronounced difficulties in the color word condition of the Stroop test and exhibited lower interference scores, indicating poor interference control. The authors concluded that the presence of rolandic discharges aggravates the course of ADHD and predisposes to a greater impulsiveness, which is usually defined as a lack of response inhibition (Nigg, 2000). In short, children with rolandic spikes show an impairment in complex executive functions, such as verbal search, use of strategy to improve verbal learning, response inhibition, and behavioral characteristics that give the impression of a dysfunction of the frontal regions. It can therefore be suggested that, despite the epileptic focus typical of BECTS being concentrated mainly in the central region, variations in its propagation may interfere with the activity of other cortical areas, such as the frontal lobe, giving rise to malfunctions that are apparently not strictly related to the primary site of the typical BECTS focus.

To confirm the behavioral findings, studies on brain volumetry confirmed anomalies in frontal lobe growth and functioning in BECTS children. Kanemura et al. (2011) examined 11 control subjects aged 4-13 years and 9 children with BECTS, two of the latter with neuropsychological impairment or behavioral problems, who were followed up for more than three years. The two children's frontal and prefrontal lobe volumes revealed a growth

impairment by comparison with the BECTS cases without deficits or the controls. The prefrontal-to-frontal lobe volume ratio also increased serially in the BECTS cases with a normal cognitive/behavioral functioning, as in controls, while it was stagnant or decreased in the BECTS cases with neuropsychological problems. Prefrontal growth also recovered more rapidly in the BECTS patient with shorter active seizure periods. So frequent spike-waves coupled with the occurrence of frequent seizures and longer active seizure periods may be associated with prefrontal lobe growth retardation, which relates to neuropsychological outcome.

3.3 Relationship between neuropsychological data and clinical features

Numerous studies investigating neuropsychological functioning in BECTS children have recently attempted to shed light on which characteristics of the EEG and which clinical variables are relevant markers of a worse cognitive outcome.

For rolandic epilepsy too, an early age of onset of the epileptic seizures correlates with a poor cognitive outcome. Piccirilli et al. (2008) suggested that seizure onset before the age of 8 years and epileptiform discharges (more than 50% of the sleep EEG recording) in several traces over more than a year are relevant markers of patients at risk of developing academic difficulties. Deltour et al. (2007) found that children with an earlier onset of seizures made more omission errors and had slower reaction times in the Continuous Performance Test.

Most authors have described improvements in neuropsychological functioning on longitudinal testing, related to a normalization of the EEG over time (Callenbach et al., 2010; Baglietto et al., 2001; D'Alessandro et al., 1990; Deonna et al., 2000; Hommet et al., 2001; Lindgren et al., 2004; Metz-Lutz et al., 1999; Northcott et al., 2007; Volkl-Kernstock et al., 2009), but there have also been reports of persistent impairments after remission of the EEG discharges (Monjauze et al., 2005).

Although some studies found that the nature of the impairments revealed by neuropsychological testing in BECTS correlated with the side of the epileptic focus (Massa et al., 2001; Piccirilli et al., 1994; Wolff et al., 2005), other studies found no relationship with the BECTS children's performance (Deltour et al., 2007; Vago et al., 2008). Studies investigating language functions using standard tests also failed to confirm any major impairment for children with a left focus (Metz-Lutz et al., 1999; Northcott et al., 2005; Staden et al., 1998; Weglage et al., 1997). Riva et al. (2007) found that children with a left-sided spike focus scored significantly worse than controls on phonemic fluency, while children with a right-sided spike focus scored significantly worse than controls in the Vocabulary subtest of the WISC-R and in the lexical comprehension test. Bulgheroni et al. (2008) found no specific influence of the side of the interictal spikes on DL performance.

Correlating the topography of the focus (in terms of the hemispheric localization and the side) with neuropsychological impairments is particularly difficult in BECTS, because spike location varies as the disorder evolves (Pinton et al., 2006) and there are reports of bilateral oscillations for the lateralized time-domain spike, suggesting a synchronized activity in a network of bilateral rolandic neurons (Lin et al., 2006). Varying spike locations on one or both hemispheres may in fact mean that BECTS should be considered as resulting from a widespread age-related hyper-excitability of the sensorimotor and latero-temporal cortices, changing its prominent location over time and leading to a functional modification that gives rise to a mild but protracted dysfunction of fine cortical processing (Kellaway, 2000). According to Metz-Lutz et al. (1999), the epilepsy appeared to disrupt response organization

rather than lateralized cognitive functions, also interfering with the development of cortical areas remote from the rolandic focus.

Some studies have correlated neuropsychological findings with the unifocal/multifocal spike location, finding that multifocal locations seem to more severely impair the cognitive efficiency of BECTS children. Multifocal anomalies seem to interfere with performance both in lexical comprehension tests and in phonemic fluency tasks, by comparison with controls (Riva et al., 2007) and had a particularly significant impact on the laterality index, with the complete loss of the right-ear advantage in favor of a symmetrical performance (Bulgheroni et al., 2008). In the work conducted by Vago et al. (2008) the majority of the under 10-year-olds (who had worse results in the CVLT) had multifocal anomalies, suggesting that the difficulties encountered might be caused by the presence of additional foci. Wolff et al. (2005) also found lower scores in cognitive tests in children with multifocal spikes. These results may mean that a widespread hyperexcitability is capable of causing more severe disruption.

The published data are not unequivocal, however, not even as concerns the correlation between spike frequency and neuropsychological functioning. Deficits in IQs correlated significantly with the frequency of spikes in the EEG (Riva et al., 2007; Weglage et al. 1997). Staden et al. (1998) reported a trend towards worse language dysfunction rates with more frequent epileptic discharges. Conversely, Massa et al. (2001) found no direct cause-and-effect relationship between the number of interictal paroxysms and cognitive symptoms, although the mean number of interictal paroxysms differed in statistical terms between their typical and complicated groups. Northcott et al. (2005) found no correlation between spike burden and difficulties in memory or phonological awareness, while Weglage et al. (1997) quantified spike frequency but did not correlate this with specific neuropsychological and language functions. Using a semiquantitative measure of spikes in EEGs recorded while awake, Staden et al. (1998) found a trend towards higher language dysfunction rates with more frequent epileptogenic discharges, whereas Bulgheroni et al. (2008) found no significant link between DL performance and interictal discharge rate, suggesting that cortical dysfunctional states depend on protracted periods of hyper-excitability leading to centrotemporal spikes, rather than on the time course (and quantity) of the spikes at the time of the DL test. It might be argued that the lack of any correlation between spike rate and neuropsychological data is due to the interval between the EEG recording on which the interictal spike rate was calculated and the neuropsychological assessment being too long to enable a detailed correlation analysis between the electrophysiological and cognitive measures, but Wolff et al. (2005) conducted a combined EEG/MEG examination chronologically very close to the neuropsychological assessment and still found no correlation between the number of spikes and the cognitive results.

4. Continuous spike and wave during slow sleep syndrome

4.1 Characteristics of EEG discharges

In electrical status epilepticus in sleep (ESES), the EEG shows a dramatic activation of epileptiform discharges during sleep, with near-continuous spike-wave discharges. It was originally believed that for a diagnosis of ESES diffuse and generalized anomalies with continuous spike-wave complexes in sleep had to occupy at least 85% of the total slow sleeping time and persist on three or more records over a period of at least 1 month (De Negri, 1997; Patry et al., 1971). The recent literature considers this definition too restrictive

and ESES-related syndromes are thought to derive from a combination of electrographic features and clinical symptoms, such as gradual cognitive and behavioral deterioration (Scheltens-de Boer, 2009). The two main representative syndromes associated with ESES are: the Landau-Kleffner syndrome, in which the EEG shows focal or multifocal spikes or spike-waves mainly in the temporal or parieto-occipital regions, which are activated in sleep; and the continuous spike and wave during slow sleep syndrome (CSWS), in which the EEG pattern is typically described as diffuse and bilateral, more rarely with a markedly asymmetrical slow wave activity over both hemispheres (Paquier et al., 2009; Rossi et al., 1999). In wakefulness, the electrographic pattern frequently shows anomalies that are focal, multifocal or diffuse, often with frontal or temporal focus (Nickels and Wirrell, 2008; Tassinari et al., 2000); some authors have reported that the frontal lobe are more involved (Nickels and Wirrel, 2008; Smith & Polkey, 2008). Eighty percent of CSWS patients have seizures, which are typically nocturnal, partial motor or generalized convulsive seizures. A characteristic of this syndrome is the presence of seizures with falls, occurring in 44% of patients (Tassinari et al., 1992). Other epileptic or paroxysmal signs include facial contractions followed by loss of consciousness, myoclonic absences (Tassinari et al., 1992), infantile spasms (Veggiotti et al., 1998) and generalized nonconvulsive seizures (Gaggero et al. in Beaumanoir et al., 1995).

CSWS syndrome is believed to be rare, with an incidence of less than 1% of all cases of childhood epilepsy (Nickels and Wirrel, 2008). The age of onset of CSWS is variable, beginning between at 1 to 14 years old, and peaking between 4 and 8 years of age (Tassinari e Rubboli, 2006). It can last from months to years, improving gradually over time, with an initial reduction in the frequency and spread of the discharges in sleep, followed by a normalization of the recordings in wakefulness, and finally by a normalization of the sleep recordings too in adolescence (Nickels & Wirrell, 2008). The evaluation of seizures is usually considered benign (Tassinari et al., 2000); in one-third of patients epilepsy persists after puberty, despite the disappearance of ESES (Scholtes et al., 2005).

4.2 Neuropsychological and behavioral profile

In CSWS it is difficult to establish the exact incidence of neuropsychological impairments because most reports describe single cases or numerically limited series and the data analyses are often not very accurate (Galonopoulou et al., 2000). For example Scholtes et al. (2005) describes the neurological and neuropsychological long-term follow-up of 10 children with global or specific cognitive deterioration and ESES-type EEG findings without specifying the case they use or providing the results in detail. Moreover, children with CSWS often have such severe behavioral disturbances in the active stage of the condition that a neuropsychological assessment becomes impossible (Veggiotti et al., 2001).

Although most patients are reported to have normal neuropsychological and motor development prior the onset of symptoms (Morikawa et al., 1995; Tassinari et al., 1992), in approximately one third of patients pre-existing neurological abnormalities are reported, such as neonatal and febrile convulsions, congenital hemiparesis, psychomotor retardation, shunts for hydrocephalus, family history for epilepsy (Galonopoulou et al., 2000). Regardless of the prior cognitive and neurological status and development, the appearance of CSWS is associated with the emergence of a new and progressive regression of global competences, with a marked impairment of IQ and behavioral abnormalities (Tassinari et al., 2000). Few papers in the past have reported on cases of CSWS without concomitant cognitive impairments (Aicardi & Chevrie, 1982; Gokyigit et al., 1986).

Attention problems and hyperactivity are prominent in CSWS patients, with deficit described in approximately two thirds of the reported case (Galonopoulou et al., 2000). There are descriptions of reduced attention span, aggressiveness, lack of inhibition (Scholtes et al., 2005; Tassinari et al., 1992; Veggiotti et al., 1998). There are also reports of bizarre behavior (Kyllerman et al., 1996; Morikawa et al., 1995), emotional lability, anxiety and phobia (Morikawa et al., 1995), and of autistic-like behavior (Bulteau et al., 1995; Kyllerman et al., 1996), although a case of CSWS with autistic regression is a rare occurrence: McVicar et al. (2005) conducted a retrospective review of children with language regression studied at their Institute for more than 12 years, finding that only 10 children had ESES, only one of whom had a history of autism and language regression.

Some works report a deterioration of language with a tendency toward expressive aphasia with lexical and syntactic difficulties, and a generally preserved comprehension (Debiais et al., 2007; MacAllister & Schaffer, 2007), learning difficulties at school, poor reasoning and short-term memory deficits (De Negri et al., 1997; Tassinari et al., 1992; 2000), and also motor impairments, such as ataxia, dystonia and dyspraxia (Maquet et al., 1995; Tassinari et al., 2000).

Roulet-Perez et al. (1993) reported clinical manifestations suggestive of a poor functioning in skills correlated to executive functions. The 4 patients showed the association of neuropsychological disorders (difficulties in verbal and non-verbal reasoning, altered temporal sequences, perseverations, reduced verbal fluency, echolalia) with behavioral disorders (lack of attention hyperactivity, impulsiveness, loss of the sense of danger, absence of inhibition, aggressiveness). Praline et al. (2003) studied the neurocognitive outcome in 7 young adults, 5 with CSWS and 2 with Landau-Kleffner syndrome, all with normal premorbid conditions. In the CSWS group only one patient still had active, treated epilepsy at the time of assessment. The neuropsychological findings in the 5 subjects led the authors to distinguish between two different groups: the first comprised two intellectually normal patients who were socially and professionally integrated; the second consisted of 3 patients who were poorly integrated because of the neurological and psychological consequences of their CSWS syndrome. They had intellectual disability, with IQs on WAIS-R indicative of a mild-moderate retardation. One of them had homogeneous mental deficiency, while the other 2 had a significantly lower non-verbal than verbal level of functioning. As for to spoken language, naming scores were normal; verbal fluency scores were pathological in 2 of the 5 patients; 3 had difficulty in sentence comprehension and 4 were deficient in reading and writing. These findings are difficult to interpret, however, because the intellectual level of these patients was low and they were behind at school. In the two subjects with a normal IQ, the author failed to identify significant frontal deficits, i.e. absence of interference in the Stroop Color Test and normal performance on Part B of the Trail Making Test. The reasons for these cognitive profiles colud be related to the topography of the interictal foci: the 5 CSWS patients studied by Praline et al. (2003) showed an epileptic focus prevalently localized in the posterior area of the brain, while the patients with dysexecutive disorder and CSWS had a frontal interictal focus during the active phase of the disorder (Roulet-Perez et al., 1993).

Kanemura et al. (2009) measured frontal and prefrontal lobe volumes using 3-dimensional MRI-based volumetry in an 11-year-old girl. Her premorbid psychomotor development was reportedly normal. After the onset of ESES, a progressive behavioral deterioration was observed, with hyperactivity, aggressiveness and disinhibition. The CSWS lasted for 5

months, the seizures first developing at the age of 5 years. The EEG abnormality recorded during ESES and in the wakeful state mainly affected the frontal region. Serial measurements (when the EEG pattern first appeared, and 6 months then 1, 2, 3 and 4 years thereafter) showed a disturbed growth in prefrontal lobe volume, and particularly in the prefrontal-to-frontal lobe volume ratio, after the appearance of the EEG pattern by comparison with FLE children with no neuropsychological disorders and 13 control subjects. The prefrontal-to-frontal lobe volume ratio increased serially in the controls and FLE children, whereas its increase declined in the patient. The ratio returned to the one seen in controls, however, after the clinical manifestations of CSWS improved. These findings provide further support for the involvement of the prefrontal cortex in CSWS, but this single case study is not enough to allow for any general conclusion to be drawn. Further studies are needed to confirm and complete these anatomical observations and extend the study of cognitive and behavioral functioning to a larger clinical sample.

4.3 Relationship between neuropsychological data and clinical features

In epileptic encephalopathies such as CSWS, the hypothesis is that the seizures or prolonged interictal epileptiform activity are responsible for the cognitive, neuropsychological and behavioral deterioration (Nabbout & Dulac, 2003). Early onset is associated with a greater functional impairment, in fact Scholtes et al. (2005) reported a better prognosis if the age of onset was 9 years or more.

The severity of ESES can vary over time between and within patients, and a direct correlation between clinical status and the spike-wave index has not been proved (Scholtes et al., 2005; VahHirtum-Das et al., 2006). As regards the localization of interictal foci, this seems to play a major part in influencing the degree and type of cognitive dysfunction in CSWS patients (Tassinari & Rubboli, 2006). CSWS patients with prominent cognitive and behavioral dysfunctions tended to have a frontal focus, while those with mainly language-related dysfunctions had a temporal focus. There is a considerable overlap between groups, however, which makes it difficult to draw clear distinctions between them (Rousselle and Revol, 1995).

With spontaneous or drug-induced improvements in the EEG findings, there is reportedly a significant but still only partial improvement on the cognitive and behavioral plane (Paquier et al., 2009; Tassinari & Rubboli, 2006). Scholtes et al. (2005) describe a good cognitive recovery after the disappearance of ESES in only 1 of 7 children, while 4 had a partial recovery. In Tassinari's study (2000), almost half (47%) of the patients with a long-term follow-up were leading a normal life, e.g. attending regular school or working; the remainder were either institutionalized or were unable to adapt properly to their working environment. It is generally assumed that the prognosis is better in patients with a shorter-lived CSWS, i.e. ESES persisting for more than two years tends to be associated with greater impact on cognitive and behavioral functioning (De Negri, 1994; Rousselle and Revol, 1995). The neuroimaging study by Kanemura et al. (2009) confirms that the duration of CSWS is a significant prognostic factor. In the work by Praline et al. (2003), this correlation was not confirmed, but the small size of their sample involved to prevent any general conclusions from being drawn. As a whole, these data are similar to those reported in the review of Galanopoulou et al. (2000) that reported a poor prognosis in half of the cases.

Treatment for CSWS aims to reverse the ESES pattern of the EEG. The goal of treatment of ESES is not only to control seizures, however, but also to improve neuropsychological function, which requires significant improvements in the encephalographic abnormalities.

5. Conclusions

Epileptic EEG paroxysms can interfere with cognitive processes. The specific nature and severity of neuropsychological problems vary according to the particular localization, diffusion and severity of EEG discharges.

The children and adolescents with epileptic anomalies involving the frontal lobe show a significant impairment of the executive abilities (abilities primarily processed by the frontal lobe), but a uniform neuropsychological and behavioral profile has yet to be established. Part of the variability could stem from the difference in the localization of epileptogenic foci within the frontal lobe, and from the tendency to spread rapidly, also to the contralateral hemisphere.

The dysfunction most frequently described is a reduced capacity for inhibitory control of previously-learned, highly-activated responses, irrespective of the type of material proposed. The majority of the neuropsychological tests used in the studies mentioned here have in common the requirement that the patient select an appropriate response and start responding, while inhibiting other, irrelevant responses. This applies to tasks that explicitly investigate these skills, but also to motor and working memory tasks.

The selective impairment of some executive skills, and the sparing of others, is further evidence of the fact that dysexecutive syndrome is not a single disorder, and executive functions depend on multiple, separate networks (Lezak et al., 2004; Stuss & Alexander, 2000), as confirmed by imaging studies (Christensen et al., 2011; Roberts & Hall, 2008).

Existing studies describing neuropsychological functioning in children with frontal epilepsies provide important information but have methodological limitations that should be addressed in future research. Such methodological implications include the size of clinical samples, clinical and epidemiological heterogeneity, psychiatric comorbidities, and the extent of neuropsychological batteries, as well as the omission of important variables related to a patient's cognitive profile (seizure severity, type of medication, lack of ecological-subjective measures indicating how patients and their families perceive their everyday functioning), which are very important and require consideration in future. Future research on larger and better-selected patient subgroups may show whether different patterns of cognitive impairment relate to different epileptogenic foci within the frontal lobe. Considering the clinical variables, we might conclude that the extent of neuropsychological impairment correlates with both the severity and the age of onset of the epileptic anomalies, that is a diffuse epileptic activity and an early age of onset have a more severe fallout on performance in neuropsychological tests. Since the onset of epilepsy can interfere with the growth of the frontal lobe and the development of the skills that it processes, future neuropsychological studies should focus on younger subjects, investigating children in preschool age, to assess their functioning profile also with a view to providing rehabilitation therapy significantly to support these skills and monitor their progress in school age.

Not having an unequivocal neuropsychological reference profile makes it necessary to conduct in-depth neuropsychological assessments to investigate each individual's functioning profile, and such assessments must also consider daily life functioning. In neuropsychological tests, a child is asked to complete a single task, within a limited time and according to more or less clear instructions concerning the start and end of the test. These conditions are very different from those of real life, where a scarcely structured setting demands decision-making and strategic processes of far greater complexity.

Adapting to daily life is even more complex, because it offers many possible solutions (also related to an individual's personal and social context), and dealing with them requires simultaneous executive processes, such as identifying relevant information and generating strategies, but also social and emotional skills, and the capacity to understand other people's points of view and signals from the environment.
The current approach is to develop so-called ecological tests using tasks similar to everyday ones to circumvent the lack of sensitivity in traditional tests (Nyhus & Barcelò, 2009).
It is also important to pay attention to qualitatively analysis of the child's performance and mistakes, which enables an assessment of the nature and efficiency of their mental processes. It is essential to observe how the proposed tasks are completed, watching how the children approach the task, what strategies they adopt, how they plan and organize their actions in order to achieve the required result, and whether or not they verify what they have done.

6. References

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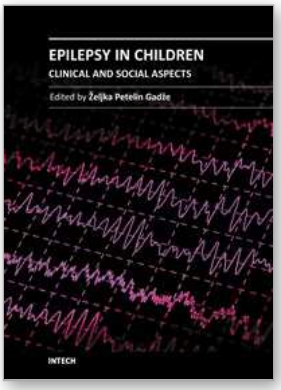

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Epilepsy is a neurological condition that accompanies mankind probably since its inception. About 400 years before Christ, the disease was already known by Hippocrates, who wrote the book â€œOn The Sacred Diseaseâ€. Classically, epilepsy has been defined as a chronic condition characterized by an enduring propensity to generate seizures, which are paroxysmal occurring episodes of abnormal excessive or synchronous neuronal activity in the brain. Out of all brain disorders, epilepsy is the one that offers a unique opportunity to understand normal brain functions as derived from excessive dysfunction of neuronal circuits, because the symptoms of epileptic seizures are not the result of usual loss of function that accompanies many disease that affect the brain. I am therefore extremely honoured to present this book. The 15 very interesting chapters of the book cover various fields in epileptology â€“ they encompass the etiology and pathogenesis of the disease, clinical presentation with special attention to the epileptic syndromes of childhood, principles of medical management, surgical approaches, as well as social aspects of the disease.

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Phone: +86-21-62489820
Fax: +86-21-62489821