Emergence and brain development of executive functions

A. Capilla[a,b], D. Romero[c], F. Maestú[a,b], P. Campo[a], S. Fernández[d], J. González-Marqués[b], A. Fernández[a,e] and T. Ortiz[a,e]

[a] *Magentoencephalography Center Dr. Pérez Modrego.* [b] *Basic Psychology II Department. Complutense University of Madrid.*
[c] *Psychology Department. University Studies Center of Talavera de la Reina. University of Castilla-La Mancha.*
[d] *Psychology Department. Camilo José Cela University. Madrid.* [e] *Psychiatry Department. Complutense University of Madrid. Spain*

Emergencia y desarrollo cerebral de las funciones ejecutivas

Summary

Development of executive functions (EF) during childhood and adolescence is closely related to frontal lobe maturation and its connections with other cortical and subcortical structures. The main maturative processes are myelination and synaptic pruning, both of which work on the brain following a hierarchical model. Different studies agree with the fact that EF emerge at the age of 6 years. However, these studies have used complex neuropsychological tests, which require appropriate functioning of several cognitive functions. This is why differential development of different EF components cannot be observed. To do so, other studies have designed simpler tasks, which only need active maintenance of information and inhibition, both basic functions for the appropriate execution of more complex EF tasks. When these simple tasks are used, an early appearance of EF can already be noticed at the age of 12 months, and there are important advances between the third and fifth year. Consequently, the idea of the frontal lobe being «functionally silent» until adolescence seems definitively discarded.

Key words: *Development. Childhood. Executive functions. Inhibition. Working memory. Prefrontal cortex.*

Resumen

El desarrollo de las funciones ejecutivas (FE) durante la infancia y la adolescencia guarda una estrecha relación con la maduración del lóbulo frontal y de sus conexiones con otras estructuras corticales y subcorticales. Los principales procesos madurativos son la mielinización y la eliminación sináptica selectiva (o poda sináptica), que actúan sobre el cerebro siguiendo un modelo jerárquico. Distintos estudios coinciden en señalar que las FE emergen evolutivamente a los 6 años de edad. Sin embargo, estos estudios han empleado tests neuropsicológicos complejos que requieren un adecuado funcionamiento de varias funciones cognitivas, por lo que no permiten apreciar el desarrollo diferencial de los distintos componentes de las FE. Para ello otros estudios han diseñado tareas más simples que únicamente necesitan un mantenimiento activo de la información e inhibición, funciones que se consideran básicas para la adecuada ejecución de tareas más complejas de FE. Utilizando estas tareas simples se pueden observar inicios de FE ya a los 12 meses de edad e importantes avances entre los 3 y los 5 años, por lo que la idea de que el lóbulo frontal es «funcionalmente silente» hasta la adolescencia parece definitivamente desechada.

Palabras clave: *Desarrollo. Infancia. Funciones ejecutivas. Inhibición. Memoria de trabajo. Corteza prefrontal.*

INTRODUCTION

The term «executive functions» (EF) has traditionally been considered as synonymous of «frontal lobe functions», since frontal lobe disease, mainly in dorsolateral prefrontal region, is frequently associated with an alteration in them. However, this relationship is not biunivocal. Thus, there are patients with posterior lesions that also cause problems in EF task execution[1].

In the same way, although there is a strong relationship between frontal lobe maturation and EF emergence during childhood and adolescence[2-5], this relationship is also not biunivocal. Thus, it has been suggested that EF development does not exclusively depend on prefrontal cortex maturation, but also on maturity and integrity of other brain regions, this being both cortical as well as subcortical[6], and of the efficient interaction between these and the prefrontal cortex[7-8].

FRONTAL LOBE DEVELOPMENT

Frontal lobe anatomic development

After birth, a series of maturative processes shape and give form to the fine anatomy of the infant's brain[6]

Correspondence:
Tomás Ortiz
Centro de Magnetoencefalografía Dr. Pérez Modrego
Universidad Complutense. Facultad de Medicina
28040 Madrid (Spain)
E-mail: cmeg@rect.ucm.es

(table 1). These processes are twofold: progressive and regressive. The progressive phenomena refer to cellular proliferation, dendritic arborization and myelination, while the regressive phenomena would mainly be neuronal death (*apoptosis*), which means regression of dendritic spines and synapsis, and selective synaptic elimination or synaptic pruning[9]. The two events that are considered maximum responsible for the brain maturation process are myelination and synaptic pruning. It has been suggested that both processes could co-occur in development, so that the space that becomes vacant as a consequence of the decreased synaptic density may be occupied by myelin[4]. These two phenomena have been related with, and are consistent with, the changes observed in magnetic resonance (MRI) studies in the cerebral white matter (myelination) and gray matter (synaptic pruning)[4].

Progressive phenomena: myelination

Myelinization greatly contributes to the improvement of brain functionality, since it produces an increase in nerve impulse conduction rate[15].

As we will comment on later, the maturative processes do not act simultaneously in all the brain regions, but follow a hierarchical model, in which the projection areas mature before the associative ones[8,11]. Thus, the last areas to acquire a «myelinated appearance» in the MRI are the white matter of the frontal, parietal and occipital lobes, which can be seem at 8-12 months[14]. During the course of the development, an increase has been observed both in volume as well as myelination of the white matter[14,16,17]. In the frontal lobe, the amount of white matter increases linearly from 4 to 13 years[16], although its myelination process and that of other association areas, such as the temporal and parietal regions, are not totally completed even until adult age[8].

Possibly, myelination plays a crucial role in the development of EF in the infant. These functions do not exclusively depend on the correct functioning of the prefrontal cortex. Rather, we should consider the prefrontal regions as one more step in a circuit that involves both cortical as well as subcortical regions[7,18,19]. Thus, EF development in the infant depends not only on specific brain region maturation (i. e., prefrontal cortex) but also on connection maturation (i. e., myelination) between them[7,8].

Regressive phenomena: synaptic pruning

During childhood, a polyneural innervation phenomenon is observed, that is, there are more synaptic connections than in the adult[20], but not all of them are functional. Thus, pruning is necessary to selectively eliminate the less relevant synapses. Therefore, those synapses that repeat will be maintained («neurons that fire together wire together»), while those that do not repeat will be eliminated[21]. In layer III of prefrontal cortex, the pruning process is continuous from 5 to 16 years of age, which is reflected in a decrease of synaptic density[11]. Decrease in synaptic density has been related with changes in the gray matter that is observed during childhood and adolescence[22].

According to Giedd et al.[16], the frontal gray matter volume increases until adolescence, where it reaches its maximum, and after which it decreases. However, Sowell et al.[4] observed a reduction in gray matter density, both in the posterior parietal cortex as well as in some frontal regions, even during childhood and adolescence. During the post-adolescent period, they observed a stabilization of these changes in the parietal cortex while the loss of gray matter continues in the superior frontal gyrus. Several authors coincide in mentioning that late decrease of the gray matter during adolescence is characteristic of the parietal and frontal regions[4,22,23]. Specifically, an even later development, which is prolonged to adult age, is produced in the dorsolateral prefrontal cortex[4].

Thus, it seems that synaptic pruning is also a fundamental process in the infant's cognitive development. Sowell et al.[24] have observed that there is a relationship between these changes in the frontal gray matter and the cognitive task performance course from 7 to 16 years of age.

TABLE 1. Maturative processes in frontal lobe

Neurons		
Number	Maximum at 2 years	Rakic, 1988[10]
Density	Maximum at birth Rapid decrease 0-6 months Slow decrease 2 years-maturity	Huttenlocher, 1979[11]
Dendritic arborization	Until 7 years, at least, in middle frontal gyrus	Huttenlocher, 1990[12]
Synaptic development		
Synaptogenesis (synaptic density)	Maximum at 12 months Gradual decrease until 16 years	Huttenlocher, 1979[11]
Synaptic pruning	Until 20 years in middle frontal gyrus	Huttenlocher, 1994[13]
Myelination	«Myelinated appearance» at 8-12 months	Paus et al., 2001[14]
	Continuous during the second decade of life	Klinberg et al., 1999[15]

Frontal lobe functional development

It was initially thought that the frontal lobe was «functionally silent» during childhood, so that the functions related with it could not be evaluated until the second decade of life[6]. The first studies that demonstrated the existence of frontal metabolism in earlier moments of development were those performed by Chugani and Phelps[25,26] with positron emission tomography (PET). These authors observed that there was an increase in the local cerebral metabolic rate for glucose in the lateral prefrontal cortex at 6 months of age and in the medial prefontal cortex at 8 months of age. The metabolic pattern was similar to that of the adult brain at 12 months of age[26].

The local cerebral metabolism for glucose in cortical regions increases from birth to 2 years, an age at which it reaches the adult levels. After this, it continues to increase until 3 or 4 years, moment in which it presents maximum metabolic rates, approximately 2.5 times greater than those of the adult brain. This high rate is maintained until approximately 9 years of age, when it begins to decline until returning to the adult levels, which it reaches during the second decade of life[25]. There is no single explanation for this increase in energetic demands during development. Two explanations that are not exclusive have been proposed, since each one of them is related with one of the two types of previously mentioned phenomena: progressive and regressive phenomena. The explanation referring to the progressive phenomena proposes that the greater metabolic rate during development is due to excessive fuel expenditure by oligodendroglias during the myelination process. The second explanation, referring to the regressive events, proposes that the synapsis excess existing during development means that there is a greater metabolic rate, that is necessary to maintain the membrane potentials[26,27]. Thus, as the synaptic density decreases, as a consequence of the pruning process of the irrelevant connections, the metabolic needs should also decrease. In fact, the marked decrease observed in metabolism during adolescence co-occurs with the reduction of the gray matter density observed during this same period.

Hierarchical model of brain development

Not all the brain regions develop at the same time. Rather, the progressive and regressive maturation phenomena follow a hierarchical model, acting first on the projection areas and then on the association ones[8,11]. Thus, the prefrontal cortex, together with the supralimbic region (parieto-temporal associative areas) are the last areas to complete their development[8].

In addition to there being a hierarchy in development, we could consider that the brain is also hierarchically organized. Within this hierarchy, the prefrontal cortex would be one of the structures that maintains the most connections with the remaining cortical as well as subcortical regions[28]. Thus, the development of the «frontal» or executive functions would not only depend on the prefrontal cortex maturation but also on the integrity and maturity of all the brain areas from which it receives inputs[2,6,8].

EMERGENCE AND DEVELOPMENT OF EXECUTIVE FUNCTIONS

Definition of executive functions

The first step in the study of EF development should be its conceptualization. However, this issue is not easy since there has been no agreement on the definition of the term up to now[1]. Most of the EF definitions list a series of cognitive processes that are supposed to be «executive». These are cognitive flexibility, goal selection, planning, monitoring, feedback use, problem solving, formulation of abstract concepts, self-control and self-consciousness[29], among many others. In fact, the EF term has become a «conceptual umbrella» since all those functions that are considered «upper order» have been included in it. This lack of specificity of the term has made it lose all operativeness[1].

One of the debates of present interest in the study of executive functions is that referring to the unity or diversity of executive functions. In a recent up-dating on the question, Miyake et al.[30] evaluated the relationship existing between three functions, considered basic for the correct performance of the EF tasks: shifting between tasks or mental set, updating and monitoring of the working memory representation, as well as inhibition of prepotent responses. The results show that these three executive functions are separable constructs but not totally independent, which would support both the unity hypothesis, that defends that the executive system is one with different components, as well as the diversity hypothesis, according to which the central executive is fractionated into different independent subsystems.

The questions that then arise are: what is common to all these EF? What makes them moderately correlated and not totally independent subsystems? According to Miyake et al.[30], there are two functions that could be the basis of this commonalities: working memory and inhibition. These two functions, besides being key milestones for adequate functioning of EF tasks, maintain a relationship between each one, so that those individuals who has better performance on working memory tests are also more effective to inhibit irrelevant information[3]. The nature of this relationship is not clear. According to some authors, both would depend on the same limited capacity system, so that an increase in demands of one of them would affect the capacity to perform the other[31]. According to others, working memory would be a primary function, while inhibition would be a secondary one[32]. Authors such as Barkley[33,34] however, would defend the contrary posture. According to the model developed by Barkley, behavioral inhibition would be essential for good functioning of four EFs: working memory, internalization of speech, self-regulation of affect-motivation-arousal and reconstitution. These four EFs have an influence on the motor system to, finally, perform a goaldirected behavior[33].

In summary, both inhibition as well as working memory seem to be basic cognitive processes for the correct performance of other functions considered executive. The study of «building-up» and evolution of inhibition and working memory in the infant could be very useful to distinguish up to what extent these processes are involved in executive functioning, increasing our understanding on the nature of the EFs in this way.

Executive function development

Most of the studies performed with classical neuropsychological tests agree in stating that the EFs emerge at 6 years of age[2]. At this age, the capacity to carry out strategic and planned behavior, a skill that has not completed its development at 12 years[25,26], appears. In regards to problem solving and hypothesis testing, which in most of the studies have been assessed by execution in the Wisconsin card sorting test (WCST), a gradual improvement has also been observed from 6 to 10 years, although performance is not comparable to that of the adult until 12 years of age[37-39]. Inhibition, or response modulation, follows a similar development to that observed in the WCST, that is, gradually improving during the middle childhood (6-10 years), reaching its maestry at 12 years[36,38]. Verbal and designs fluency seem to be a later function, whose development is not completed until the first adolescent period (12-15 years)[38,40]. According to Welsh et al.[39], there are three stages in the EF development, at 6 years, at 10 years and in adolescence (from 12 years on) that would be the development times in which maturation of the different EF is consistently observed. Table 2 shows the main functions that mature at these ages, according to different studies.

The results obtained in these studies show that EF development is a multistage process, that is, the functions considered to be executive mature in different ways and at different times, analogously to the previously mentioned hierarchy in the brain development[8,40].

However, these studies have an important limitation, inherent to all study on EF. The neuropsychological tests used to assess these capacities have a construct validity that is somewhat questionable. The EF tasks are non-specific, since there are several executive and cognitive skills in general, underlying their correct execution[30]. Thus, some classical neuropsychological tests, such as the WCST or Tower of London/Hanoi test (TLH), depend on different functions for their execution, so that it is not clear what executive function the infant has developed in order to be able to perform them. Rather, the non-specific nature of these tasks would include the need to develop different executive functions that are inseparable in regards to the score obtained, before being able to complete them successfully.

TABLE 2. EF that matures at 6 years, 10 years and in adolescence, according to different studies

6 years	
Simple planning	Welsh et al., 1991[39]
Simple inhibition	Klenberg et al., 2001[40]
10 years	
Hypothesis testing	Welsh et al., 1991[39]
Impulse control	Welsh et al., 1991[39]
Adolescence (> 12 years)	
Complex planning	Welsh et al, 1991[39]
Goal-directed behavior	Anderson et al., 2001[41]
Verbal fluency	Welsh et al., 1991[39]
	Klenberg et al., 2001[40]

Consequently, each author characterizes the nature of these tasks with a different name, as can be observed in table 3, in which the factorial structure of EF found by different authors is seen. The content of the factors found has important parallelisms, since the factors found in the same row are made up, approximately, by the same test, while those that do not have parallelisms with the other studies are mainly constituted by tests only used in this study. In spite of these parallelisms in the essence, the manners are very different, since, as can be observed, the terms used for the description of similar factors are quite varied[38,39,41]. This is especially outstanding in the third factor since, although the only test in the three studies that saturates in it is the Tower of London/Hanoi (TLH), each author refers to it differently. This lack of agreement in terminology is possibly the reflection of the lack of a solid conceptual framework of the EF.

Emergence of the executive functions: working memory and inhibition

As has already been mentioned, most of the studies that have used classical neuropsychological EF tests state that the EFs appear at 6 years[2]. However, other studies in which simpler tests that require basic working memory and inhibition abilities have been used, mark an earlier beginning, already finding EF rudiments in the first year of life and important advances between 3 and 5 years.

Development from 8 to 12 months

We could consider that the first milestone in EF development is object permanence, skill described by Piaget[42]. Acquiring this skill supposes that the infant is capable of creating a mental representation of the world surrounding him/her and of maintaining this information in his/her mind. It has been suggested that the underlying function of this skill is working memory[43]. Its evaluation has been carried out by delayed response tasks,

TABLE 3. Comparison of the result of principal component analysis (PCA) performed in three different studies about EF development

Welsh et al., 1991[39]	*Levin et al., 1991*[38]	*Anderson et al., 2001*[41]
Fluency and speeded response		Attentional control and processing speed
Hypothesis testing and impulse control	Preservation/disinhibition	Monitoring/planning
Planning (TLH)	Planning and strategy formulation (TLH)	Problem solving (TLH)
	Semantic association and concept formation	
		Accuracy
		Organizational abitities

Those factors with a similar content are shown in the same row. TLH: Tower of London/Hanoi.

equivalent to the A-not-B task used by Piaget[44], in which an object is hidden in one of two possible location (one, on the right; another, on the left). Some seconds after, the infant should point to where the object has been hidden, which means that he/she should hold this information in his/her mind for a few seconds. It has been suggested that this task requires both holding the information in mind (working memory) as well as inhibiting a prepotent response (pointing to the location in which the object was found in the previous trial). When the infant searches for the object in the location in which it was found in the previous trial, it is considered that an «A-not-B error» has been committed, which is analogue to the perseverative errors observed in patients with frontal lobe damage[3].

Object permanence appears at approximately 8 months and develops during the period ranging from 8 to 12 months of age, in which 2 second increases in delay time is observed each month. This period is a time of important maturative changes in the infant, both cognitive as well as cerebrally. Considering the cognitive development timing, according to Piaget's theory[42], the infant is in substage IV of sensorimotor period from 8 to 12 months. In this substage, besides the appearance of object permanence, the infant also would acquire the capacity to coordinate means and goals, and, according to Piaget, intelligence would appear[44]. It is possible that the appearance of the capacity to coordinate means and goals would be one more reflection of the emergence of working memory, since, carrying out this coordination requires maintenance and manipulation of the internally represented information. On the other hand, we could also consider it the most rudimentary state of planning and problem solving, functions considered executive, that require an internal representation of the goals and the means to achieve them, as well as their manipulation and monitoring.

During this period, a large amount of maturative changes is also produced in the infant's brain, involving, in great extent, the frontal cortex. As we have already commented, the local cerebral metabolic rates for glucose increases at 8 months in the medial prefrontal cortex, as well as in most of the frontal cortex[25]. In this period, a marked growth of length and extension of the dendritic branches of the in pyramidal neurons layer III of the dorsolateral prefrontal cortex is also observed and these reach their maximum extension at 12 months[45]. Given that the cortex layer III, together with layer II, are formed by efferent pyramidal neurons that project on other cortical regions, their maturation could be related with an improvement in communication between prefrontal cortex and other cortical areas. Finally, the progress in delayed response task execution has been related with changes in the electrical activity pattern of the frontal cortex, as well as in coherence of the EEG between the frontal and parietal cortex[46]. This latter fact agrees with the idea that adequate execution of working memory tasks does not only depend on activation of local structures but also on communication between them by the formation of extensive neural networks[7,19]. Specifically, involvement of a frontoparietal network in spatial working memory tasks has been suggested[19].

Development from 3 to 5 years

From 3 to 5 years, children experience important improvements in tasks that only need an active maintenance of information (working memory) and inhibition for their performance. This type of task is known as task switching paradigms and it has been suggested that its performance requires, in great extent, the functioning of the dorsolateral prefrontal cortex[3]. Table 4 shows some of the task switching tests that have been used to detect the emergence of basic executive capacities in younger children. Since it has fewer requirements of other functions than the classical EF neuropsychological tests, it may detect the emergence of simple EF more accurately.

Different authors, using these tasks, have found that 3 year old children have a reminiscent error of the «A-not-B error», that is, they fail to inhibit the ongoing mental set and redirect their attentional focus toward the new set. This fact may be observed in the Zelazo's card sorting task[49,50], similar to the Wisconsin card classification task (WCST), with exception that in the former, they are only two dimensions to sort: color and shape. Three year old children are not capable of inhibiting the current perceptive dimension in favor of the new one, even when the examiner names the card according to the new dimension[3]. However, in conditional discrimination tasks, in which change from one dimension to another is not necessary, and thus, does not have the irrelevant dimension inhibition component, 3 year old children do have correct execution[49]. It has been suggested that the dorsolateral prefrontal cortex activity only requires change when the attentional focus must be redirected to a different dimension, and not for the performance of changes within one same dimension[3].

After 4 years of age, approximately, children begin to experience important progresses in this type of tasks[3]. At this age, improvement in EF tests correlates with the improvement observed in Mind Theory tests. It has been suggested that this simultaneous advance in both types of tasks could be related with the maturation of the frontal white matter of the right hemisphere[55]. Approximately at this age, from 4.5 to 5 years, a growth spurt has also been in the maturation of the EEG coherence in the frontal lobe of the right hemisphere which, however, has not been found in the left hemisphere[56].

In summary, the age period ranging from 3 to 5 years seems to be a time of important brain and cognitive changes related with the EF. According to Piaget's terminology[42], the infant would go from being pre-operational to being operational. One of the milestones that mark this change is the acquisition of «liquid conservation», a phenomenon that consists in the fact that a certain amount of liquid continues to be the same regardless of the shape of the container in which it is in. When the infant acquires this skill, he/she is no longer dominated by the more perceptually salient dimension (in this case, the height of the container), and begins to reason in terms of representations. In neuropsychological terms, this change would be produced by the acquisition of skills to maintain more than one thing in the mind and to be able to inhibit a prepotent response tendency simultaneously[3]. Although these skills emerge in early childhood and develop rapidly during middle childhood, their maturation process is prolonged, also observing progresses, although slower, during adolescence[3,41]. Development, although even incomplete, of the working memory and inhibition skills during childhood could partially contribute to the previously commented advances in the EF tests, such as the WCST or TLH. A growing investigation area is the study of brain functioning in working memory and inhibition tasks during childhood by the use of neuroimaging techniques, especially functional magnetic resonance (fMRI). These studies could supply complementary information on the brain structures involved in EF task performance during childhood.

TABLE 4. Tasks with a task-switching format, that require active maintenance of information and inhibition for performance[3,55]

Day-night task	Gerstadt et al., 1994[47]
Luria tapping test	Luria, 1966[48]
Zelazo card sorting task	Zelazo et al., 1995[49]
	Zelazo et al., 1996[50]
Appearance-reality task	Flavell, 1986[51]
	Falvell, 1993[52]
Theory of mind and false-belief tasks	Hogrefe et al., 1986[53]
	Gopnik & Astington, 1988[54]

Working memory and inhibition in childhood and adolescence: studies with functional magnetic resonance

Working memory

Working memory studies performed with fMRI show that the cerebral regions activated during the performance of these tasks in children are basically the same as those activated in adults[5,19,27]. The differences found between them refer to intensity of the signal more than its site. According to Casey et al.[27], activation intensity would be two or three times greater in children. It has been suggested that this increase in signal intensity could be due to the fact that the task is proportionally more difficult in children, since they would be exposed to a greater working memory demand in comparison to adults[27]. In fact, an increase in signal intensity as the memory load increases has been observed in adults[57]. On the contrary, in other studies, greater brain activation has been found in adults during the performance of a visuospatial working memory task[19].

Another important finding is that, even though the areas activated in children and adults are similar, there are also small activations in other prefrontal regions in the children, which is revealed by a more diffuse activity pattern. This pattern could be the reflection of an immature cortical organization, in which the synaptic pruning process of the less functional connections has not yet been completed[27].

As we have commented, the regions activated in children in comparison with the adults are basically the same. However, there are some differences that should be stressed, such as the activation of the right cingulate cortex in adults that does not appear in children. This lack of activation of the cingulate cortex in children could be related with the persistence in errors that they show in the task execution[5].

Finally, it is important to consider that the performance of these working memory tasks does not only recruit prefrontal regions. During visuospatial working memory task execution, an important contribution of the parietal cortex is also observed[5,19]. It has been suggested the visuospatial working memory task execution does not only depend on local computations within specific regions, but also on communication between them[19]. In conclusion, according to Luciana and Nelson[7], adequate use of working memory should necessarily involve interactions between prefrontal cortex and several cortical and subcortical regions, as the associated parietal and temporal regions, the thalamus, and the basal ganglia. According to these authors, three processes participate in development of working memory. In the first place, structural maturation of the specific brain regions. In the second place, refinement of local circuits within these regions. It is likely the synaptic pruning participates to achieve this refinement. Finally, extensive, large scale, neural networking would be formed and would integrate the interactions between different local circuits. There is the possibility that the myelinization and maturation process of the white matter contributes to the improvement of communication between prefrontal cortex and different cortical and subcortical regions underlying working memory.

Inhibition

Inhibition is not a unitary process. According to different authors, inhibitory control would be made up by different dissociable aspects. The first dissociation establishes a difference between inhibition in attention and inhibition in action. Inhibition in attention refers both to selective attention as well as change of attentional focus from one perceptive dimension to another. In the first, inhibition of attention to irrelevant stimuli is required, while in the second, inhibition of one of the dimensions is required, which would make it possible to focus attention on the other dimension. On the other hand, in inhibition action would include change from one response pattern to another one and inhibition of a prepotent response tendency[3]. There is evidence of a dissociation between the neural circuits of both types of inhibition. Thus, in inhibition attention would recruit anterior areas of the dorsolateral and ventrolateral prefrontal cortex[3]. Regarding action inhibition, inhibition of a prepotent response has also been related with activation of dorsolateral and ventrolateral prefrontal cortex areas, while change from one response pattern to another would be more related with posterior areas of the dorsolateral prefrontal cortex and immediately posterior premotor cortex[3]. One of the key processes in the change of a response pattern is the selection process, which refers to the resolution of the competition between different representations. According to different authors, the left inferior prefrontal cortex would be highly involved in this process[58,59].

According to Casey et al.[18], the two inhibition in action subtypes, change of a response pattern to another and inhibition of a prepotent response tendency, would be, in turn, dissociable. Thus, there would be three inhibition types in all that would correspond with different types information and/or with different of stages cognitive processing: inhibition in stimuli selection (equivalent to inhibition in attention), in the response selection (change from one response pattern to another) and in response execution (inhibition of a prepotent response tendency). There is evidence of dissociations between these three inhibition types in children with different diseases. Thus, for example, children with attention-deficit hyperactivity disorder (ADHD) would not show problems in inhibition in response selection, but would show it in the selection of stimuli, which has been related with distractibility symptoms, and in response execution, related with impulsiveness symptoms[18,33].

Finally, it is important to take into account the contribution of Barkley[33]. According to him, behavior inhibition, equivalent to inhibition in action, would be made up of three interrelated processes: inhibition of a prepotent response for a stimulus, capacity to stop an answer underway, that would permit a delay period to decide what answer to give and, finally, protection of the delay period and of the self-directed responses of stimuli and competitive responses, which is known as interference control, that has been widely studied under the Stroop effect paradigm.

Studies on inhibitory control performed with fMRI show inconsistent results, which may be partially due to the fact that different types of behavior inhibition have been studied[60]. For these studies, mainly two types of tasks have been used. On the one hand, *go/no-go* tasks, that require inhibition of a prepotent response tendency before it is begun[61] and, on the other, *stop-signal* tasks, that require inhibition of an ongoing response, once it has already begun[62].

Casey et al.[61] show that, during the performance of a *go/no-go* task, the same cerebral regions are activated, both in children and in adults. These are the orbitofrontal cortex, the right anterior cingulate cortex, the middle frontal gyrus (MFG) and the inferior frontal gyrus (IFG). Differences between children and adults lie in the activation volume, which is greater in MFG and IFG in children. Other authors, however, using this same task, have found that activation is greater in the middle frontal gyrus (MFG) and superior frontal gyrus (SFG) of the left hemisphere in children, while it is greater in the IFG of the left hemisphere in adults[60]. On the other hand, during the performance of *stop-signal* tasks, differences in the regions activated on the basis of age have been observed. While IFG activation of the right hemisphere and caudate nucleus of the same hemisphere has been seen in adolescents, there is greater activation of the IFG of both hemispheres and the MFG of the left hemisphere in adults.

It is not clear what these activation differences between children and adults are due to. In some cases, they show greater activation volume of the prefrontal regions in children, while in others, they show lower activation in comparison to adults. In the same way as for working memory, it has been suggested that the more extensive activation found in children would reflect a diffuse activity pattern, possibly due to inefficient recruitment of the brain regions involved. As age increases, the selectivity of the regions recruited would also increase, so that there would be a greater focal activation of specific regions involved in response inhibition[18,60].

CONCLUSIONS

Lack of a conceptual framework of the EF is one of the main obstacles in the study of its development. As we have commented, lack of agreement on what are the EFs and which are their main components has important repercussions on how to evaluate them. For this reason, neuropsychological tests, designed, in the beginning, to assess the effects of brain damage on cognitive functions, have been used. These tests are non-specific, since the functioning of several EF is necessary for their correct performance. In spite of this, these tasks are useful for the purpose they were designed for, that is, to determine if brain damage has affected the EFs, since, if any of its components are altered, this would be reflected in the test score. However, the non-specificity of these tasks makes them less useful when the purpose is to study the EF evolutive emergence and development, since it is extremely difficult, if not impossible, to relate the test score with the acquisition of any specific EF component. Thus, studies that use this methodology, more than describing the development of the EF components, describe the development of the capacity to perform certain EF tests. Thus, for example, evolution of capacities is described as fluidness or maintenance of the set, which, more than essential components of the EF, could be considered as abilities derived from their adequate functioning. It is important to discriminate what are the essential components of the EF from which are the skills derived from them because, if not, we continue increasing the «conceptual umbrella» of the EF.

Thus, although the neuropsychological tests are useful for that which they were designed, they are not so useful for the study of EF emergence and development. For this purpose, it seems to be more useful to design simple cognitive tasks that require the use of basic functions, such as working memory or inhibition, that is believed to be involved in the performance of complex EF tasks[30,32].

The study of the emergence and development of these capacities is a previous step for the investigation of other questions, such as, for example, what consequences do a traumatic brin injury (TBI) that occurred during the neurocognitive development process have on EF development. Before being able to understand how the development is transformed as a consequence of an external agent, we must know how the development process naturally develops[6]. Brain damage does not have the same consequences on the mature brain of an adult person as on the immature brain of a infant, since the latter is continuously developing, so that we must analyze the consequences from a dynamic approach. According to the Dennis model[63,64], after damage to a developing brain, there is not only loss of present functions but also, and what is more important, difficulty to acquire future functions, so that the children will progressively become delayed in the achievement of appropriate evolutive gains for their age. They will become increasingly distanced from what their normal development should be. It is important to know how the pattern of normal development during childhood and adolescence is, since the impact of the damage will be different based on whether the cognitive ability in question is emerging, developing, or already established.

Considering that the EF are the last ones to complete their development, it is likely that they are especially vulnerable to early brain damage that disrupts them before they have naturally emerged. In the literature, there are many single case reports that reflect this delayed deficit of the EF after a TBI in an early moment of development[65-67]. The study of the effect that early TBIs have on the future acquisition of late maturation functions, such as EFs, may help us to understand something more on the normal development process, and if this follows a hierarchical model in which EF maturation and that of the frontal lobe play a fundamental role in the organization and integration of the remaining cognitive functions and brain regions[68].

Finally, studying the infant's brain, we have the opportunity of seeing, briefly, how human cognition has been «built up» and its maximum phylogenetic advance: the prefrontal cortex, which «is important for so many divers cognitive functions and for so much of what makes us proud to be human beings»[3] (p. 494).

REFERENCES

1. Tirapu Ustárroz J, Muñoz Céspedes JM, Pelegrín Valero C. Funciones ejecutivas: necesidad de una integración conceptual. Rev Neurol 2002;34(7):673-85.
2. Anderson V. Assessing executive functions in children: biological, psychological, and developmental considerationst. Pediatr Rehabil 2001;4(3):119-36.
3. Diamond A. Normal development of prefrontal cortex from birth to young adulthood: cognitive functions, anatomy, and biochemistry. En: Stuss DT, Knight RT, editores. Principles of frontal lobe function. New York: Oxford University Press, 2002; p. 466-503.
4. Sowell ER, Thompson PM, Tessner KD, Toga AW. Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: inverse relationships during postadolescent brain maturation. J Neurosci 2001;21(22): 8819-29.
5. Thomas KM, King SW, Franzen PL, Welsh TF, Berkowitz AL, Noll DC, et al. A developmental functional MRI study of spatial working memory. Neuroimage 1999;10(3 Pt 1):327-38.
6. Anderson V, Northam E, Hendy J, Wrennall J. Developmental neuropsychology: a clinical approach. Hove: Psychology Press, 2001.
7. Luciana M, Nelson CA. The functional emergence of prefrontally-guided working memory systems in four to eight year old children. Neuropsychologia 1998;36(3):273-93.
8. Stuss DT. Biological and psychological development of executive functions. Brain Cogn 1992;20(1):8-23.
9. Pfefferbaum A, Mathalon DH, Sullivan EV, Rawles JM, Zipursky RB, Lim KO. A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. Arch Neurol 1994;51(9):874-87.
10. Rakic P. Specification of cerebral cortical areas. Science 1988;241:170-6.
11. Huttenlocher PR. Synaptic density in human frontal cortex-developmental changes and effects of aging. Brain Res 1979;163(2):195-205.
12. Huttenlocher PR. Morphometric study of human cerebral cortex development. Neuropsychologia 1990;28:517-27.

13. Huttenlocher PR. Synaptogenesis, synaptic elimination and neural plasticity in human cerebral cortex. En: Nelson CA, editor. Threats to optimal development: integrating biological, psychological, and social risk factors. Hillsdales: Erlbaum, 1994; p. 35-54.
14. Paus T, Collins DL, Evans AC, Leonard G, Pike B, Zijdenbos A. Maturation of white matter in the human brain: a review of magnetic resonance studies. Brain Res Bull 2001;54(3): 255-66.
15. Klingberg T, Vaidya CJ, Gabrieli JD, Moseley ME, Hedehus M. Myelination and organization of the frontal white matter in children: a diffusion tensor MRI study. Neuroreport 1999;10(13):2817-21.
16. Giedd JN, Blumenthal J, Jeffries NO, Castellanos FX, Liu H, Zijdenbos A, et al. Brain development during childhood and adolescence: a longitudinal MRI study. Nat Neurosci 1999;2(10):861-3.
17. Steen RG, Ogg RJ, Reddick WE, Kingsley PB. Age-related changes in the pediatric brain: quantitative MR evidence of maturational changes during adolescence. Am J Neuroradiol 1997;18(5):819-28.
18. Casey BJ, Tottenham N, Fossella J. Clinical, imaging, lesion, and genetic approaches toward a model of cognitive control. Dev Psychobiol 2002;40(3):237-54.
19. Klingberg T, Forssberg H, Westerberg H. Increased brain activity in frontal and parietal cortex underlies the development of visuospatial working memory capacity during childhood. J Cogn Neurosci 2002;14(1):1-10.
20. Purves D, Lichtman JW. Elimination of synapses in the developing nervous system. Science 1980;210:153-7.
21. Casey BJ, Giedd JN, Thomas KM. Structural and functional brain development and its relation to cognitive development. Biol Psychol 2000;54:241-57.
22. Jernigan TL, Trauner DA, Hesselink JR, Tallal PA. Maturation of human cerebrum observed in vivo during adolescence. Brain 1991;114:2037-49.
23. Sowell ER, Trauner DA, Gamst A, Jernigan TL. Development of cortical and subcortical brain structures in childhood and adolescence: a structural MRI study. Dev Med Child Neurol 2002;44(1):4-16.
24. Sowell ER, Delis D, Stiles J, Jernigan TL. Improved memory functioning and frontal lobe maturation between childhood and adolescence: a structural MRI study. J Int Neuropsychol Soc 2001;7:312-22.
25. Chugani HT, Phelps ME. Maturational changes in cerebral function in infants determined by 18FDG positron emission tomography. Science 1986;231(4740):840-3.
26. Chugani HT, Phelps ME, Mazziotta JC. Positron emission tomography study of human brain functional development. Ann Neurol 1987;22(4):487-97.
27. Casey BJ, Cohen JD, Jezzard P, Turner R, Noll DC, Trainor RJ, et al. Activation of prefrontal cortex in children during a nonspatial working memory task with functional MRI. Neuroimage 1995;2(3):221-9.
28. Gazzaniga MS, Ivry RB, Mangun GR. Cognitive neuroscience : the biology of the mind. New York: WW Norton, 1998.
29. Estévez-González A, García-Sánchez C, Barraquer-Bordas L. Los lóbulos frontales: el cerebro ejecutivo. Rev Neurol 2000;31(6):566-77.
30. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex «frontal lobe» tasks: a latent variable analysis. Cognit Psychol 2000; 41(1):49-100.
31. Cohen JD, Servan-Schreiber D. Context, cortex, and dopamine: a connectionist approach to behavior and biology in schizophrenia. Psychol Rev 1992;99:45-77.
32. Pennington BF, Bennetto L, McAleer O, Roberts RJ. Executive functions and working memory: theoretical and measurement issues. En: Lyon GR, Krasnegor NA, editores. Attention, memory and executive function. Baltimore: Paul H Brookes Publishing Co, 1996; p. 327-48.
33. Barkley RA. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. Psychol Bull 1997;121(1):65-94.
34. Barkley RA. Linkages between attention and executive functions. En: Krasnegor NA, editor. Attention, memory and executive function. Baltimore: Paul H Brookes Publishing Co, 1996; p. 327-48.
35. Becker MG, Isaac W, Hynd GW. Neuropsychological development of non-verbal behaviors attributed to the frontal lobes. Dev Neuropsychol 1987;3:275-98.
36. Passler MA, Isaac W, Hynd GW. Neuropsychological development of behavior attributed to frontal lobe functioning in children. Dev Neuropsychol 1985;1:349-70.
37. Chelune GJ, Baer RA. Developmental norms for the Wisconsin Card Sorting test. J Clin Exp Neuropsychol 1986; 8(3):219-28.
38. Levin HS, Culhane KA, Hartman J, Evankovich K, Mattson AJ. Developmental changes in performance on tests of purported frontal lobe functioning. Dev Neuropsychol 1991; 7(3):377-95.
39. Welsh MC, Pennington BF, Groisser DB. A normative-developmental study of executive function: a window on prefrontal function in children. Dev Neuropsychol 1991; 7(2):131-49.
40. Klenberg L, Korkman M, Lahti-Nuuttila P. Differential development of attention and executive functions in 3 to 12 year old Finnish children. Dev Neuropsychol 2001;20(1):407-28.
41. Anderson V, Anderson P, Northam E, Jacobs R, Catroppa C. Development of executive functions through late childhood and adolescence in an Australian sample. Dev Neuropsychol 2001;20(1):385-406.
42. Piaget J. The psychology of intelligence. Londres: Routledge & Kegan Paul, 1950.
43. Goldman-Rakic PS. Topography of cognition: parallel distributed networks in primate association cortex. Annu Rev Neurosci 1988;11:137-56.
44. Piaget J. The child's construction of reality. Londres: Routledge & Kegan Paul, 1955.
45. Koenderink MJT, Ulyings HBM, Mrzljiak L. Postnatal maturation of the layer III pyramidal neurons in the human prefrontal cortex: a quantitative Golgi analysis. Brain Res 1994;653:173-82.
46. Fox NA, Bell MA. Electrophysiological indices of frontal lobe development: relations to cognitive and affective behavior in human infants over the first year of life. Ann N Y Acad Sci 1990;608:677-704.
47. Gerstadt C, Hong Y, Diamond A. The relationship between cognition and action: performance of 3,5-7 year old children on a Stroop-like day-night test. Cognition 1994; 53:129-53.
48. Luria AR. The higher cortical functions in man. New York: Basic Books, 1966.
49. Zelazo PD, Reznick JS, Piñon DE. Response control and the execution of verbal rules. Dev Psychol 1995;31: 508-17.
50. Zelazo PD, Frye D, Rapus T. An age-related dissociation between knowing rules and using them. Cogn Dev 1996; 11:37-63.

51. Flavell JH. The development of children's knowledge about the appearance-reality distinction. Am Psychol 1986; 41:418-25.
52. Flavell JH. The development of children's understanding of false belief and the appearance-reality distinction. Int J Psychol 1993;28:595-604.
53. Hogrefe J, Wimmer H, Perner J. Ignorance versus false belief: a developmental lag in attribution of epistemic states. Child Dev 1986;57:567-82.
54. Gopnik A, Astington JW. Children's understanding of representational change and its relation to the understanding of false belief and the appearance-reality distinction. Child Dev 1988;59:26-37.
55. Perner J, Lang B. Development of theory of mind and executive control. Trends Cogn Sci 1999;3(9):337-44.
56. Thatcher RW. Cyclic cortical reorganization during early childhood. Brain Cogn 1992;20(1):24-50.
57. Braver TS, Cohen JD, Nystrom LE, Jonides J, Smith EE, Noll DC. A parametric study of prefrontal cortex involvement in human working memory. Neuroimage 1997;5:49-62.
58. Thompson-Schill SL, D'Esposito M, Aguirre GK, Farah MJ. Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation. Proc Natl Acad Sci USA 1997;94(26):14792-7.
59. Poldrack RA, Wagner AD, Prull MW, Desmond JE, Glover GH, Gabrieli JD. Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. Neuroimage 1999;10:15-35.
60. Tamm L, Menon V, Reiss AL. Maturation of brain function associated with response inhibition. J Am Acad Child Adolesc Psychiatry 2002;41(10):1231-8.
61. Casey BJ, Trainor RJ, Orendi JL, Schubert AB, Nystrom LE, Giedd JN, et al. A developmental functional MRI study of prefrontal activation during performance of a *go/no-go* task. J Cogn Neurosc 1997;9:835-47.
62. Rubia K, Overmeyer S, Taylor E, Brammer M, Williams SC, Simmons A, et al. Functional frontalisation with age: mapping neurodevelopmental trajectories with fMRI. Neurosci Biobehav Rev 2000;24(1):13-9.
63. Dennis M, Wilkinson M, Koski L, Humphreys RP. Attention deficits in the long term after childhood head injury. En: Michel ME, editor. Traumatic head injury in children. New York: Oxford University Press; 1995; p. 165-87.
64. Dennis M. Language and the young damaged brain. En: Boll T, Bryant BK, editores. Clinical neuropsychology and brain function: research, measurement and practice. Washington: American Psychological Association, 1989; p. 85-124.
65. Marlowe WB. The impact of a right prefrontal lesion on the developing brain. Brain Cogn 1992;20:205-13.
66. Grattan LM, Eslinger PJ. Long-term psychological consequences of childhood frontal lobe lesion in patient DT. Brain Cogn 1992;20(1):185-95.
67. Williams D, Mateer CA. Developmental impact of frontal lobe injury in middle childhood. Brain Cogn 1992;20(1): 196-204.
68. Thatcher RW. Maturation of the human frontal lobes: physiological evidence for staging. Dev Neuropsychol 1991; 7(3):397-419.