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Inhibition, set-shifting and working memory in Global Developmental Delay preschool children

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Abstract

Executive functions (EFs) allow to planning and voluntarily and autonomously produce targeted behaviors, in unusual or complex conditions in which the automated response schemes are not appropriate or sufficient to achieve behavior goal. The aim of this study was to evaluate EFs in preschool children presenting with Global Developmental Delay (GDD).
Fifty-two preschool children participated in this study: 20 GDD children

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and 32 typical developing children (TDC) as control group, enrolled in the schools of Campania and Sicily Regions.
All subjects underwent evaluation of the executive functioning through the administration of the Battery for the Assessment of Preschool Executive Functions (BAFE) and the Behavior Rating of Executive Function-Preschool Version (BRIEF-P).
The two groups were comparable for age and gender. GDD children showed significantly lower scores in all BAFE subscales and significantly higher in all BRIEF-P subscales compared to TDC controls.
EFs are integrated with each other and as many functions are the essential basis for the other basic skills as well as basis for more complex cognitive skills. During childhood, EFs' difficulties tend to influence not just a single area/expertise but have a global impact that extends to management, development, planning and daily living.

Keywords: Executive functions; BAFE; BRIEF-P; Global Developmental Delay.

1. Introduction

Global Developmental Delay (GDD) in early childhood can affect both cognitive functionality and adaptive behavior development. When the delay is primarily concerned with cognitive function, the child may be relatively adequate in the social environment, even with the limitations arising from its cognitive delay. When the delay mainly concerns the ability to control one's behavior, the child may find it difficult to maintain sufficient social and relational adaptation and integrate effectively in the school and family context (Lezak, 2004).

Motivational ability, planning, behavior modulation, ability to complete an action program, identification of functional strategies to achieve the goal, problem solving, flexibility, monitoring and self-assessment of behavior in relation to results, change of task or behavior in the light of emerging information are all complex behaviors defined as "executive functions". Such abilities allow to planning and voluntarily and autonomously produce targeted behaviors, in unusual or complex conditions in which the automated response schemes are not appropriate or sufficient to achieve behavior goal (Jurado & Rosselli, 2007). Executive functions, therefore, configure a set of skills that act systemically, integrating each other in relation to the nature and complexity of the task, making a person able to implement successfully independent behavior, purposeful and pragmatically functional (Lezak, 2004).

Cognitive and executive functions express two different cerebral functioning modalities. Cognitive functions allow to "know" the world, executive functions allow to "operate" and to "move inside". However, while a cognitive impairment mainly affects the specific impaired skills, an executive impairment may compromise the whole repertoire of non-automatic finalized behaviors. Moreover, executive integrity is essential for cognitive productivity, especially for attentive, mnesic and problem-solving tasks that involve planning, systematic and specific strategies and behavior monitoring (Lezak, 2004). In other words, executive functions are highly integrated functions that modulate the "lower level" cognitive processes, as well as the targeted behavior and the processes of adaptation to the environment (Alvarez & Emory, 2006).

In the literature, there is a general agreement on the role of executive functions in adaptive behavior, but there is not as much consensus on their articulation and even on the theoretical construct as such.

According to some authors, executive functions represent a unitary central system (Barkley, 1997; Salthouse, 2005). According to others, they derive from different control processes, independent and organized in modules (Stuss & Levine, 2002). According to others, still, they would configure separable skills, but united by a shared common factor and selectively sensitive to brain damage (Miyake, Friedman, Emerson, Witzki, Howerter, & Wager, 2000).

Traditionally, the frontal regions, especially the prefrontal ones, have been considered as the neuro-anatomo-functional structures that subtend both cognitive and executive functions, at the most integrated levels and act as a general superstructure of brain functioning. However, the most recent lesional studies and functional neuroimaging data (PET, fMRI), while confirming the main role of prefrontal areas, do not fully support the historical exclusive association between executive functions and frontal lobes and, even less, the concept of a single undifferentiated central control system of intentional behavior supervision. Rather, they refer to a network of anatomically and functionally independent attentive control processes that are interrelated, organized flexibly and supported by different distributed networks both within the frontal regions and within the posterior areas (Stuss & Alexander, 2007).

The frontal regions present connections with many cortical and subcortical areas, and with brainstem areas and are the only regions able of integrating the information of the external environment with the emotional and motivational dimensions that support direct action to a goal. They are, however, a component of a systemic activity involving multiple cortical structures, including posterior heteromodal areas, and subcortical structures (basal ganglia, subcortical components of the limbic system), circuits thalamic, cerebellum and brainstem (Monchi, Petrides, Strafella, Keith, Worsley, & Doyon, 2006). Even non-frontal patients, in fact, may manifest executive disorders. The most accredited neuropsychological tests as executive tests, such as Wisconsin Card Sorting Test, Verbal Fluency and Stroop are sensitive to non-specific frontal damage and may be poor even in non-frontal patients (Alvarez & Emory, 2006).

The frontal lobes, therefore, are not the only brain region responsible for such highly integrated and articulated functions and their participation in the executive processes probably must be considered as a necessary but not sufficient requirement. Executive functions, therefore, should be redefined as a “macro construct” with more synergistic sub-processes, each with specific competences, supported by different cortico-subcortical, anterior and posterior regions (Alvarez & Emory, 2006).

Miyake and colleagues (2000) found evidence for three moderately correlated executive functions in adults: working memory, inhibition and shifting. Such abilities emerge during the first 3 years of life from early simple skills (Garon, Bryson, & Smith, 2008). Further, these simpler components become integrated into the complex processes that characterize mature executive functions abilities. Therefore, more complex executive functions, such as shifting and planning, are constructed from earlier developing executive functions (Collins & Koechlin, 2012).

2. Aims and hypothesis

The main purpose of the study was to evaluate executive functions in GDD preschool children compared against a control group, with particular reference to attentive flexibility, inhibitory capacity, set-shifting and working memory visuospatial skills.

3. Materials and methods

3.1. Participants

Fifty-two preschool children participated in this study (age range 3 - 6 years). During the period of June-July 2016, 20 children (11 males, 9 females) in preschool age (between 3.1 years and 5.11 years, average age 4.56 ± .89) presenting with GDD, in accordance to international guidelines of DSM-5 (American Psychiatric Association, 2013), were enrolled at the Clinic of Child and Adolescent Neuropsychiatry of the University of Campania “Luigi Vanvitelli”, at the “Study Center of Scoliosi” SRL, at the ONLUS “Fondazione Casa dei Giochi”. Exclusion criteria were the presence of cognitive disability (IQ < 70), epilepsy and chromosomal abnormalities.

A comparison group of 32 TDC (15 males, 17 females, between 3.1 years and 5.11 years, average age 4.47 ± .77) was enrolled in the schools of the Campania and Sicily Regions.

3.2. Materials and Procedures

All subjects underwent evaluation for the executive functioning through the Battery for the Assessment of the Executive Functions in preschool (BAFE) (Valeri, Stievano, Ferretti, Mariani, & Pieretti, 2015) and Behavior Rating of Executive Function-Preschool Version (BRIEF-P) (Gioia, Espy, &

Isquith, 2014). The administration took place in a familiar setting, in a quite atmosphere, without distractors, ensuring the best performance of the children.

3.2.1. Battery for the Assessment of Preschool Executive Functions

The BAFE (Valeri *et al.*, 2015) is a clinical tool in Italy in the field of evidence available for neuropsychological assessment in children. It consists in four tasks investigating inhibition, flexibility and visuospatial working memory.

1. Shifting tasks: *Card Sort* (Valeri *et al.*, 2015). Children were introduced to two boxes that had rectangular slots cut in the top and target cards (e. g. red bear, blue house) to the front of the boxes. In the "shape game" the examiner presents a series of cards (red and blue bear and houses) and instructed children to place all the bears in the box with the red bear and to place all the houses in the box with the blue house. After five consecutively correct trials, the experimenter announced that they would stop playing the shape game and now play the "color game". All the red things would go in the box with the red bear affixed and all blue things would go in the box with the blue house affixed. The total number of correct incompatible post witch trials was recorded.
2. Inhibition tasks: *Day and Night* "Stroop-like day-night task" (Carlson, 2005; Valeri *et al.*, 2015). After a preliminary conversation about when the sun rises and it is day and when there are the moon and the stars in the sky and it is night, the examiner asks the children to say "day" when they saw a black paper with a white moon drawing and stars and say "night" when they saw a white paper with a drawing of a yellow sun. Accuracy (number correct out of 16) was recorded.
3. Set-shifting tasks: *Pattern Making Test* (Attentive Flexibility, Valeri *et al.*, 2015). Children were shown a sequence of 18 colored circles and they were asked to say the name of each color. The examiner says "See that he creates a pattern: blue-blue-red, blue-blue-red" emphasizing the words in a rhythmic way. Then the examiner asks the child to try to create exactly the same pattern using a set of red and blue magnets. No feedback is provided during the activity. The score is given by the number of correct triplets (six blue-blue-red).
4. Working memory task: *Spin the Pots* (Valeri *et al.*, 2015). In this task the child was asked to place an object (a red ring) in each of the eight different pots arranged on a tray. The tray was then covered with a

scarf and spun around. The child was then asked to lift the scarf and choose a pot. Each time the child chose a baited pot, the sweet or the object was put into a small reward envelope for the child to keep. The procedure was repeated until eight sweets had been found or after 15 trials had been conducted (whichever was sooner). Performance was rated by number of trials required to find all eight objects.

The tests are simple and brief and sometimes fun, capturing the interest and curiosity of the little ones. The ease and brevity of administration favored a peaceful examination even with younger or less collaborating children. A low level of difficulty characterizes the items of the battery in order to perform evaluative screening of children with levels of medium and medium-low executive control. In order to identify the subject's position with respect to normative data, a raw score was assigned for each single trial and for each EFs subdomain and then was converted according to percentile scores. This procedure allowed comparing two performances of the same child within two different distributions for different subdomains.

3.2.2. Behavior Rating Inventory of Executive Function – Preschool Version

The BRIEF-P was filled out by children's parents and/or teachers with the aim of evaluating executive functions from 2 years to 5.11 years, even in natural settings (home, school) (Gioia *et al.*, 2014). It is a screening tool for the identification of executive dysfunction. The development profile was defined on the basis of the attribution of the raw scores that was then converted into percentile scores and T scores. The normative tables for scales, indexes and Global Executive Composite score were differentiated on the basis of age, sex and who compiled the questionnaire (Appendix A for the parent, B for the teacher). The interview expressed the parent/teacher's point of view about daily executive functioning. Consisting of 63 items divided into 5 theoretically independent and empirically derived clinical scales measuring: inhibition (I), shift (S), emotions regulation (ER), working memory (WM) and planning/organization (PO). The scale of Incoherence and Negativity are included.

In addition to the scales, three broader indices was associated: the inhibitory self-control (ISCI) derived from the sum of inhibition (I) and emotion regulation (RE); the flexibility (FI) derived from the sum of the shift (S) and regulation of emotions (RE); the emerging metacognition (MEI) derived from working memory (WM) and planning/organization (PO). A Global Executive Composite score (GEC) was also considered.

4. Data analysis

Chi-square and the t-test analysis were used in order to compare the GDD and TDC groups for age, sex distribution and EFs evaluation. A p value $\leq$ .05 was considered as statistically significant for all analyses. All statistical analyses were performed by SPSS statistical package.

5. Results

The two children groups are comparable by age (t-test (50) = .39; p = .70) and sex (χ^2 (1) = .32; p = .57). Table 1 shows the results of the two groups on BAFE and BRIEF-P. Overall, GDD children, compared to healthy controls, showed significantly lower scores in all the BAFE sub-scales and statistically significant higher scores in all the BRIEF-P sub-scales (Tab. 1). Therefore, compared to the TDC group, the GDD group showed significantly fewer executive abilities in all the dimensions examined: inhibition, flexibility and visuospatial working memory.

Table 1- *Means, standard deviations, and comparisons between means of executive functions parameters by children with Global Developmental Delay and by typical developing children*

	GDD		*TDC*				
	M	*SD*	*M*	*SD*	*t- test*	*df*	*p-value*
BAFE (card sort)	30.6	33.4	56.6	41.7	2.3	50	.023
BAFE (day and night)	19.8	21.9	58.5	35.3	4.4	50	< .001
BAFE (pattern making test)	50.1	46.4	82.2	28.9	3.1	50	.003
BAFE (spin the pots)	30.9	22.7	44.6	21.4	2.2	50	.033
BRIEF-P T score (I)	57.1	16.7	46.0	7.4	3.3	50	.002
BRIEF-P T score (S)	64.8	15.9	46.8	7.4	5.5	50	< .001
BRIEF-P T score (ER)	64.6	17.6	44.7	6.2	5.9	50	< .001
BRIEF-P T score (WM)	56.9	20.0	44.6	3.4	3.4	50	.001
BRIEF-P T score (PO)	54.5	10.2	45.9	3.8	4.3	50	< .001
BRIEF-P T score (ISCI)	58.6	17.2	45.2	7.1	3.9	50	< .001
BRIEF-P T score (FI)	63.8	17.9	46.3	8.6	4.8	50	< .001
BRIEF-P T score (EMI)	59.3	12.9	44.8	3.3	6.1	50	< .001
BRIEF-P T score (GEC)	58.3	14.1	44.5	4.8	5.1	50	< .001

GDD: Global Developmental Delay group; TDC: typical developing children group; df: degrees of freedom; BAFE: Battery for the Assessment of the Executive Functions in preschool; BRIEF-P: Behavior Rating of Executive Function-Preschool Version; (I): inhibition; (S): shift; (ER): emotions regulation; (WM): working memory; (PO): planning/organization; (ISCI): inhibitory self-control; (FI): flexibility; (EMI): emerging metacognition; (GEC): Global Executive Composite.

6. Discussion

The present preliminary study highlights a significant impairment of the executive functioning in the early stages of development in GDD children, compared to TDC age-matched group. These findings supported the hypothesis of a close relationship between executive competences and cognitive development especially in childhood.

At a qualitative approach, in the Card Sort test, both the TDC and GDD children gave perseverative responses when they were asked to place the cards using a new criterion and abandoning the criterion of the form to move to the color. In both groups, the highest number of errors was recorded in children aged 3.1 years and 3.9 years. With increasing age, the perseverative responses decreased, especially in the TDC group. In the same age group, children presented significant difficulties in maintaining attention for the times required by the task. This last finding agrees with other previous researches that document a difficulty in the attentive maintenance still present in children around 6 years (Smirni, Oliveri, Turriziani, Di Martino, & Smirni, 2018).

The Day & Night test showed a significant reciprocal influence between basic and complex functions, between attention, cognitive flexibility and inhibitory capacity. In TDC children, both the youngest and the oldest group understood the tasks and said “day” when they saw the moon and “night” when they saw the sun. However, the youngest group frequently failed to control and inhibit the interference of the most automatic response (say “day” when the sun is out) and to give an intentionally “wrong” answer. The interferences control was more consistent in the oldest group. Moreover, the TDC group showed to be able to correct the wrong answers in an increasingly low time with increasing age. The youngest children needed some extra time both to provide the answer and to correct errors.

Among GDD children, most of those between the ages of 3.1 and 3.9 failed to perform the test both for difficulties in verbal language and for excessive adherence to the concrete that did not allow understanding the concept of “opposite”. These children did not perform the training correctly or, despite the training, performed the whole test wrong saying “sun” when they saw the sun and “moon” or “night” when they saw the moon.

At this age the percentage of errors far exceeds correct answers. Moreover, the ability to correct and evaluate the error was poor. Globally, as the chronological age increases, the number of those who correctly carry out the trial increases and errors were reduced, both in typical and global developmental delay children. In any case, this test showed a mismatch between typical and global developmental delay groups according to chronological age.

The test of the triplets of circles evaluates the attentive flexibility, the ability of visuospatial orientation, and the ability to organize an action plan. Also in this trial the differences between the two groups were significant in favor of the TDC group.

The proof "A round of jars", measuring the visuospatial working memory, is configured as a visual search in which the number of attempts to find tokens increases the most more the efficiency of the performance is deficient. Both the control group and the clinical group are able to trace the first tokens consecutively and not to choose the "empty" jar. The more the number of tokens to be found is reduced, the greater the possibility of falling into error. The search strategies were more structured in the typical development children and less in the global developmental delayed children even if the distribution remains uniform between the two groups. In all the tests the clinical group obtained a lower score for chronological age compared to the reference control sample.

BRIEF-P data also showed greater homogeneity in scores in typical development children (TDC control group) but not in GDD. Moreover, in the GDD group, the results showed greater variability around the mean compared to greater homogeneity in the control group. In all the tests the emotional and motivational factor has an impressive impact. Children with good interpersonal skills and a good degree of self-esteem perform better performances. Among neurodevelopmental disorders, there are many different conditions with executive function alteration that generally were not well explored such as sleep-related breathing disorders (Esposito, Carotenuto, & Roccella, 2011; Esposito, Antinolfi, Gallai, Parisi, Roccella, Marotta *et al.*, 2013), cognitive impairment (Esposito & Carotenuto, 2010; 2014), learning disabilities (Esposito *et al.*, 2011; Carotenuto, Esposito, Cortese, Laino, & Verrotti, 2016) autism (Precenzano, Ruberto, Parisi, Salerno, Maltese, Vagliano *et al.*, 2017), personality disorders (Sperandeo, Picciocchi, Valenzano, Cibelli, Ruberto, Moretto *et al.*, 2018) and it could be possible speculating the involvement of or exinergic system and/or projections (Messina, Di Bernardo, Viggiano, De Luca, Monda, Messina *et al.*, 2016; Chieffi, Carotenuto, Monda, Valenzano, Villano, Precenzano *et al.*, 2017; Chieffi, Messina, Villano, Messina, Esposito, Monda *et al.*, 2017; Villano, Messina, Valenzano, Moscatelli, Esposito, Monda *et al.*, 2017; Messina, Bitetti, Precenzano, Iacono, Messina, Roccella *et al.*, 2018; Messina, Monda, Sessa, Valenzano, Salerno, Bitetti *et al.*, 2018). In this picture, many tools may be considered to rehabilitate the executive functioning such as the transcranial direct current stimulation (tDCS), as the transcranial magnetic stimulation (TMS) and behavioral therapy (Turriziani, Oliveri, Bonnì, Koch, Smirni, & Cipolotti, 2009; Turriziani, Smirni, Oliveri, Semenza, & Cipolotti, 2010; Smirni, Turriziani, Mangano, Cipolotti, & Oliveri, 2015; MacPherson, Healy, Allerhand, Spano, Tudor-Sfetea, White *et al.*, 2017; Smirni, Turriziani, Mangano, Bracco, Oliveri, & Cipolotti, 2017; Maltese, Romano, Cerroni, Russo, Salerno, Gallai *et al.*, 2018; Smirni, Beadle, & Paradiso, 2018; Smirni, Smirni, Di Martino, Cipolotti, Oliveri, & Turriziani, 2018).

7. Conclusions

In GDD emerge adaptive problems do not always exclusively due to a cognitive defect. Rather these difficulties of production and self-management of purposeful behavior are traced to an impairment of executive functions that should ensure appropriate responses to new situations.

On the neurorehabilitation field, the attention to the disexecutive dimension may be a crucial premise for the construction of specific intervention programs for a wider scholastic, relational and social integration.

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