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Assessment of the executive functions of moderate preterm children in preschool age

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ABSTRACT

This study assesses EF and socioemotional development in 30 MPT children between 4 and 6 years, comparing them with 31 FT children. Working Memory was assessed with Digit Span and Corsi Block, verbal inhibitory control and cognitive flexibility with The Shape School Test, visuomotor inhibition with Go/No-Go and socioemotional development with SDQ for parents. In our study, MPT preschoolers had a poorer working memory, inhibitory control and verbal cognitive flexibility, and more emotional problems compared. Our results suggest that there is no safe gestational age in prematurity, for this reason, EF of preterm children should be evaluated at an early age, so early intervention plans can be implemented, preventing preterm from entering primary education in disadvantage.

KEYWORDS
Executive functions; moderate preterm; preterm's emotional problems

According to the World Health Organization (WHO, 2018), a child is considered premature when it is born before 37 weeks of gestation, considering that term gestation lasts between 37 and 42 weeks of gestational age. However, as it is a very heterogeneous condition, the stratification of the categories of prematurity is still not consensual and, therefore, there is a great heterogeneity of results that hinder the definition of guiding Therefore, according to WHO, prematurity can be classified into three subcategories: extreme premature (<28 weeks of gestation); very premature (28–31 weeks); and, the less consensual, moderate to late premature (32–37 weeks of gestation). This original classification joined moderate and late premature babies in the same group although the risk of subsequent consequences of moderate prematurity is higher than for late (Allotey et al., 2017; Scheuchenegger et al., 2013). Different authors addressed this question with different classifications. Moster, Lie, and Markestad (2008) used classified premature babies as extreme (23^{+0}–27^{+6} weeks); very premature (28^{+0}–30^{+6} weeks); moderate (31^{+0}–33^{+6} weeks); and late (34^{+0}–36^{+6} weeks). Likewise, Kuzniewicz, Parker, Schnake-Mahl, and Escobar (2013) considered as moderate preterm babies born between the 31^{+0} and 33^{+6} weeks, and as late premature babies born between the 34^{+0} and 36^{+6} weeks.

The concern with specifying the weeks of gestational age at birth is due to the importance of understanding the risks to which the child is exposed, with an inverse relationship between gestational age and the risk of morbidity and mortality in neonatal care (Martin, Hamilton, Osterman, Curtin, & Matthews, 2015).

Premature birth can have a significative impact on physical, cognitive, psychosocial and economic functioning that affect children, parents and communities closer to the child, in the short and long term (for a review Luu, Mian, & Nuyt, 2017; Stockman, 2010). Although the incidence and severity of pathology are lower in moderate preterm (MPT) and late preterm infants than in extreme or very preterm infants, the risk is real and affects the life of this population at long-term (Shankaran & Natarajan, 2016; Trembath, Payne, Colaizy, Bell, & Walsh, 2016).

Premature birth in the developing brain

Since brain development begins in the third week of pregnancy with the differentiation of embryonic cells and continues until at least until the end of adolescence (Lenroot & Giedd, 2006; Stiles & Jernigan, 2010), the probability of brain injury in perinatal period and the number of neurological morbidities for life are substantial (Saigal & Doyle, 2008). As a result of these events and possible structural and functional changes, this population is more exposed to cerebral palsy, neurosensory deficits, intellectual disability, seizures and severe disabilities that affect its ability to work even in adulthood (Saigal & Doyle, 2008; Stockman, 2010). The diffuse lesion of the white matter seems to be the most frequently observed lesion in the neuroimaging of premature newborns (e.g., Volpe, 2003; Volpe, 2009). Because it is in the third trimester that there is a significant increase in dendritic afforestation, synaptogenesis and other developmental processes in the prefrontal cortex (Huttenlocher & Dabholkar, 1997; van den Heuvel et al., 2015), the transition from the uterine to an artificial environment, associated with the high immaturity of prefrontal circuits, makes them

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more vulnerable to disruption due to pre or perinatal events (Lenroot & Giedd, 2006). Therefore, a prefrontal lesion in children leads to a more diffuse deficit that interferes with the age-appropriate acquisition of executive skills, such as the inhibition of overbearing responses, and may not significantly affect other aspects of intellectual development (Anderson, Damásio, Tranel & A. Damásio, 2013). Even in the absence of an identified brain injury, children born before 37 weeks of gestational age tend to present less anisotropy on diffusion tensor images (Huppi et al., 1998).

Executive functions

According to Lezak (1982), executive functions (EF) are the set of skills needed to establish objectives, plan and implement plans efficiently, fundamental to autonomous, creative, constructive and social behavior. They are, therefore, independent top-down mental processes interconnected by underlying processes that allow us to manipulate ideas, think before acting, anticipate consequences, resist to impulses and maintain the focus (Diamond, 2013; Miyake et al., 2000).

Inevitably, EF are crucial in almost all aspects of our lives (Diamond, 2013), like school preparation and success (Blair & Razza, 2007; Schmitt, Purpura, & Elicker, 2019) and for mental health (e.g., Pennington & Ozonoff, 1996). The most common EF associated disorder is ADHD (Lindstrom, Lindblad, & Hjern, 2011), characterized by difficulties in regulating attention, difficulties in concentration, excessive motor activity and difficulties in impulse control (APA, 2014). It may be of inattention type, hyperactivity type, or a mixed type (APA, 2014).

In scientific research, the definitions of EF refer to three core processes: working memory, inhibitory control and cognitive flexibility (Baddeley, 1986; Diamond, 2013; Miyake et al., 2000; Taylor & Clark, 2016). Indeed, this three-factor model for EF has been confirmed for adolescent and older children, but in preschoolers, the findings differ, with single (Hughes, Ensor, Wilson, & Graham, 2009; Wiebe, Espy, & Charak, 2008; Wiebe et al., 2011) or two-factor models (Miller, Giesbrecht, Müller, McInerney, & Kerns, 2012) emerging as the best-fit models. According to Usai, Viterbori, Traverso, and De Franchis (2014), inhibition appears, in 5 and 6-years old children, as an independent EF component apart from a working memory-flexibility factor. Cognitive flexibility, in simple response sets, emerges between 3 and 4 years of age, but children in this age range have difficulty switching when rules become more complex, extending the time needed to improvements in this skill (Espy, 1997; Zelazo, 2006). More complex cognitive flexibility tasks also depend on working memory and inhibition and so the ability to complete them matures later (Cepeda, Kramer, & Gonzalez de Sather, 2001).

Although EF skills in adults may be primarily subserved by frontal regions, there are data to suggest that frontoparietal connections are crucial in the EF skills of children.

Working memory is the ability to represent and manipulate a limited amount of information for a very short period (Baddeley, 1986). Deficits in working memory are often correlated with difficulties in school, particularly in learning to read, understanding the content read, developing vocabulary, writing, arithmetic reasoning and understanding complex instructions (Dehn, 2008). The activation of working memory in children with a mean age of 6 years activates a diffuse pattern of activity in frontoparietal brain networks, particularly in the prefrontal ventromedial cortex, the upper parietal cortex, and the anterior cingulate cortex (Kharitonova, Winter, & Sheridan, 2015).

Inhibitory control is defined as the ability to control attention, thoughts, emotions and behaviors in order to ignore irrelevant stimuli (Miyake et al., 2000). Inhibitory control is essential to activate selective and sustained attention, facilitates flexibility and behavioral change, and allows us to adapt to social rules (Diamond, 2013). In one study about neurophysiological activation of 5-year old children in a go/no-go task, it was found that children's brains activated structures such as the ventromedial, the dorsomedial and the ventrolateral of the prefrontal cortex (bilaterally) (Lahat, Todd, Mahy, Lau, & Zelazo, 2009). Réveillon and colleagues (2013) found that children between 6 and 7 years of age activate, when performing a Go/No-Go task, frontotemporal regions, including the lower prefrontal circumvolution, the upper temporal circumvolution, the insula and the *globus pallidus*, mainly from the right hemisphere. Consequently, inhibitory control deficits are essentially associated in children with attention-deficit and hyperactivity disorder (Barkley, 1997; Chmielewski et al., 2019), poorer school performance (Blair & Razza, 2007), and eating disorders (Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016).

Cognitive flexibility is the ability to switch fluidly between objectives, tasks and stimuli, implying the activation of the working memory to manipulate the latter perspective, and the inhibitory control for its inhibition (Diamond, 2013). In a study about the neural correlates of emerging cognitive flexibility in preschool age, the authors reported greater activation of the left dorsolateral prefrontal cortex (Li, Grabell, Wakschlag, Huppert, & Perlman, 2017). In older children, the activation occurs in the dorsolateral prefrontal cortex, the right ventrolateral, the left parietal cortex, the anterior cingulate cortex and the striate cortex (Rubia et al., 2006).

Despite the lack of a clear picture of the relationship between these three factors, it is known that the first years of life have a critical role in the development of EF, which reinforces the importance of evaluation at the preschool level. Specifically, it is between 3 and 5 years of age that major improvements occur in both inhibition, working memory and cognitive flexibility abilities (Garon, Bryson, & Smith, 2008).

Implications of moderate prematurity in executive functions and socio-emotional development

EF are especially important to study since they are considered a mediator of the effect of gestational age on adaptive function, school performance and behavioral symptoms (Loe, Feldman, & Huffman, 2014; Baron, Kerns, Müller, Ahronovich, & Litman, 2012; Taylor & Clark, 2016).

Due to the lower risk of physical problems, the literature about the EF development of MPT and low-risk premature children is scarce, so more studies are needed to draw robust conclusions (Baron et al., 2012; Hodel et al., 2017; Van Houdt, Oosterlaan, Wassenaer-Leemhuis, Van Kaam & Aarnnoudse-Moens, 2019; Vohr, 2013).

According to Johnson and collaborators (2015), moderate to late premature children presented, at 2 years of age, a higher risk of moderate to severe cognitive and executive deficits in relation to their term peers. Mulder, Pitchford, Hagger, and Marlow (2009) conducted a meta-analysis to assess the impact of prematurity on the development of EF children over 2 years old and found that the size of the effect of studies assessing inhibitory control with Go/No-Go tasks is highly correlated with gestational age, with the smallest effect in preterm infants with more gestational weeks. In this study, working memory also seems to be affected by preterm birth, even when socio-demographic factors are controlled. More specific studies, such as that of Vicari, Caravale, Carlesimo, Casadei, and Allemand (2004) suggest deficits in visuospatial working memory in preterm infants from 29 to 34 weeks of pregnancy with low weight.

The systematic review of Allotey and colleagues (2017), that included 64,061 children through the analysis of 74 studies, concluded that difficulties in working memory and behavioral regulation seem to increase with age in MPT births (Allotey et al., 2017), which may be related to the increased demands of the environment and the disregard of possible difficulties of these children, as happens at later gestational ages (Baron et al., 2012). The effect of gestational age on the working memory remained intermediate even after school age (Allotey et al., 2017).

According to Scott and collaborators (2012), MPT children with worse performance in working memory and inhibitory control tasks exhibit more negative behaviors in school settings, increasing up to nine times the probability of a combined type of ADHD diagnosis, up to five times the probability of meeting inattention-type ADHD criteria and up to 11 times the probability of experiencing difficulties in socioemotional regulation. In the meta-analysis of Allotey and collaborators (2017), the largest association between ADHD and gestational age occurred in moderate prematurity, with a 3.7 OR (1.8; 7.7). However, according to Wolke (1998), premature children with less than 1500 g at birth tend to present an attentional type of ADHD, which is also supported by other authors who consider that MPT children, or children with less than 2500 g, diagnosed with ADHD, have higher means for inattention, but not for hyperactivity (Johnson & Marlow, 2011).

When assessing 82 children born with 34 or fewer weeks of gestational age, Loe, Heller, and Chatav (2019) found that, in premature populations, deficits in working memory and inhibitory control are twice as common in relation to behavioral impairment.

Academic success is lower among MPT children, with a greater need for curricular adaptations in the area of special education (Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008). At 5 years of age, 63% of MPT children do not reach a good level of general school performance (Huddy, Johnson, & Hope, 2001; Quigley et al., 2012). Therefore, between 25 to 39% of MPT children with developmental delay or specific deficits have symptoms of internalization and externalization (Potijk, de Winter, Bos, Kerstjens, & Reijneveld, 2015), with a higher prevalence of socio-emotional problems (Arpi & Ferrari, 2013; Johnson et al., 2018; Potijk et al., 2015) emotional reactivity and somatic complaints (Potijk et al., 2015).

To our knowledge, the number of studies focusing on the EF, especially on cognitive flexibility, of MPT children of preschool age is scarce. Even when it is considered a larger age spectrum, there are not enough studies in MPT population that allow us to draw strong conclusions (Van Houdt et al., 2019). However, given the increased risk of brain injury in the inner capsule and upper longitudinal fascicle (Kelly et al., 2016; Walsh, Doyle, Anderson, Lee, & Cheong, 2014), cognitive flexibility may be an important skill to assess at an early age.

The current study

Taking into account the revised literature, this study defined as a preliminary objective (1) determining whether children born between 31 and 33 gestational weeks, currently aged between 4 and 6 years, present lowers scores on EF tasks than their full-term (FT) peers; and as a second objective (2), to verify whether MPT children present more emotional and behavioral symptoms.

The specific aims of the present study were as follows:

(1A) Compare the mean scores of the instruments that evaluate the verbal working memory of MPT children and their FT peers; (1B) Compare the mean scores of the instruments of visual working memory of MPT children and their FT peers; (1C) Compare the performance in verbal inhibitory control measures of MPT group and FT group; (1D) Compare the performance in the variables extracted from visuomotor inhibitory control instruments of MPT and FT peers; (1E) Compare the performance in verbal cognitive flexibility tasks of MPT children and FT children; and

(2) Compare the scores of MPT children and FT children's Strengths and Difficulties Questionnaire (SDQ) subscales filled by parents, more specifically: (2A) Compare the total of difficulties; (2B) Compare the scores of emotional problems subscale; (2C) Compare the scores of behavioral problems subscale; (2D) Compare the scores of hyperactivity and attention deficit subscale; (2E) Compare the scores of interaction with peers subscale; and (2F) Compare the scores of pro-social skills subscale.

Method

Participants

Two groups of Portuguese native children aged between 4 and 6 years were collected to this study.

The experimental group consisted of 30 MPT children born between 31^{+0} and 33^{+6} gestational weeks collected in two hospitals, one of Almada and other of Funchal, Portugal. The children were selected based on the records provided by the institutions, and the parents were contacted in person during a hospital consultation or by telephone. Out of a total of 43 contacted MPT children who met the defined inclusion criteria, we obtained the consent of 30 subjects. The 13 subjects who did not want to enroll were equivalent to the 30 who did based on demographic variables.

The control group, composed of 31 FT children, was collected in preschools of the Lisbon district, Portugal, and paired with the experimental group based on age and gender. None of the FT controls were excluded on the basis of exclusionary criteria.

The inclusion criteria were (1) the birth of the child between 31 and 33 weeks of gestational age for the experimental group and 37 or more weeks for the control group; and (2) being between 48 and 83 months of age at the time of the assessment. The exclusion criteria were (a) the existence of diagnosed mild or severe neurological lesions; (b) identified malformation syndromes; (c) intellectual deficit or learning difficulties already identified; (d) severe motor or sensory deficits; and (e) a performance below the 25th percentile in the Raven Colored Progressive Matrices.

Procedure

All children underwent a neuropsychological assessment of EF and socioemotional development. Procedures and measures were approved by the Scientific Committee of Portuguese Catholic University and by Scientific and Ethics Committees of both hospitals where participants were contacted. Written informed consent was obtained from all parents or guardians.

Sociodemographic data

Following the existing literature about the theme, a questionnaire was prepared for parents in order to allow the sociodemographic characterization of this population, formulated to determine the gestational age and birth weight (only in the experimental group) at birth, the current age of the child, the occurrence of postnatal health complications, the existence of pathologies, and the maternal age at birth and current education level.

General cognitive functioning

General cognitive functioning was assessed with the Portuguese version of Raven Colored Progressive Matrices (RCPM; Raven, 1947; Simões, 1995) for children. RCPM assesses the ability of children to deduce logical relationships, one of the main constituents of Charles Spearman's general intelligence and g-factor general intellectual ability (McCallum, Bracken, & Wasserman, 2001).

None of the participants had a performance below the 25th percentile in RCPM.

Working memory

Verbal working memory was assessed with Digit Span subtest from WISC-III (Wechsler, 2003), in direct and backward order. For the evaluation of visual working memory we used Corsi Block from Bateria de Avaliação Neuropsicológica de Coimbra (BANC; Simões et al., 2016), a nine cubes board used to evocate visual sequences in direct order. As Corsi Block from BANC does not have items in backward order, the sequences from Digit Span backward order (WISC-III) were used.

Inhibitory control

Verbal inhibitory control was assessed with The Shape School Test (Espy, 1997; Rato, Ribeiro, & Castro-Caldas, 2017). The test follows a short story format with four experimental conditions that are presented in a fixed order: (A) control; (B) inhibition; (C) cognitive flexibility; and (D) inhibition and flexibility. To assess inhibitory control was used the time and correct answers of the conditions B and also considered condition D (Espy, 1997; Rato et al., 2017).

Visuomotor inhibitory control was measured through the Go/No-Go task of Early Years Toolbox (EYT; Howard & Melhuish, 2017), an IOS application for iPad's in a game format in which the child must touch the screen when seeing a fish ("go" stimulus), but never when passing a shark ("no-go" stimulus). In addition, each stimulus appears for about 1.500 ms (for children aged 4 years) or 1.000 ms (for children aged 5 or 6 years) with an interval between stimuli of 1.000 ms (Howard & Melhuish, 2017). From this test, we were able to extract the reaction time and the number of correct answers. For the assessment of the sensitivity to the stimulus, we applied Signal Detection Theory (SDT) and calculated the d' [Z (Go accuracy) − Z (False Alarm)] (Van der Kellen, Nunes, & Garcia-Marques, 2008).

Verbal cognitive flexibility

Verbal cognitive flexibility was assessed analyzing the time it took to name the stimuli (in seconds) and the number of correctly named stimuli in conditions C and D of The Shape School Test (Espy, 1997; Rato et al., 2017).

Socioemotional development

A Portuguese version of Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997; Fleitlich, Loureiro, Fonseca, & Gaspar, 2005) for parents of 4 to 17 years old children was used to evaluate the socioemotional development of both groups. The SDQ is a brief behavioral screening questionnaire with 25 closed-ended answer questions: "Not true"; "Somewhat true"; and "Certainly true". The quotation of the SDQ implies the sum of the scores for the calculation of six subscales of the questionnaire: (1) Emotional Problems; (2) Conduct Problems; (3) Hyperactivity and Inattentional; (4) Peer Relationship Problems; (5) Prosocial Behavior; and (6) the Total Difficulties by adding the scores of the first four subscales (Goodman, 1997).

Statistical analysis

Qualitative variables (sex, educational level of the mother and inhibitions of C and D condition of SS) were analyzed with Chi-square (X^2). To assess the differences in

Table 1. Neonatal, child and mother characteristics of MPT and FT.

Measure	Moderate preterm	Full term	Statistic	p	Effect size	CI
M (SD) Age (months) ($n_{MPT} = 30$; $n_{FT} = 31$)	66.20 (8.019) [49;79]	66.39 (6.407) [51;76]	$t(61) = -0.101$	0.920	$d = 0.026$	[−3.899; 3.525]
% Male ($n_{MPT} = 30$; $n_{FT} = 31$)	60.0	61.29	$X^2(1) = 0.011$	1.000	$\Phi = -0.013$	
M (SD) Gestational weeks ($n_{MPT} = 30$; $n_{FT} = 31$)	32.20 (0.847)	39.18 (0.983)	$t(56) = -29.018$	<0.001	$d = -7.232$	[−7.460; −6.497]
M (SD) Weight (g) [minimum; maximum] ($n_{MPT} = 30$)	1495.48 (229.567) [998; 1900]					
M (SD) Maternal age at birth [minimum; maximum] ($n_{MPT} = 30$; $n_{FT} = 29$)	30.80 (6.703) [17;42]	33.86 (5.674) [24;46]	$t(57) = -1.891$	0.064	$d = 0.493$	[−6.305; 0.181]
Maternal education ($n_{MPT} = 30$; $n_{FT} = 29$)	(%)	(%)				
Primary (1st cycle)	6.5	0	$X^2(6) = 11.138$	0.084	Cramér's $V = 0.442$	
Primary (2nd Cycle)	13.3	3.2				
Lower secondary	23.3	6.5				
Upper secondary	20	29				
Bachelor	30	45.2				
Master	6.7	0				
Doctoral	0	3.2				

quantitative variables (such as children's age, gestational weeks, mother's age, correct answers and reaction times) between groups, independent samples t-Student tests were conducted in *Statistical Package for the Social Sciences* 23.0 (SPSS 23.0; IBM Corp, 2015). Results were significant at $p < 0.05$. To analyze the magnitude's effect of the differences, Cohen's d was calculated for variables analyzed with the t-Student tests and classified according to the table proposed by Cohen (1988), and the Fi coefficient (φ) and Cramer's V for dichotomous variables analyzed with the Chi-square. Subsequently, we studied the association between the variables Gestational Age and subscales Emotional Problems and Problems with Pairs, with Pearson's Correlation Coefficient (Marôco, 2014).

Missing data

The sociodemographic questionnaires of two children in the control group were not returned so the age of the mother at birth and her education level were not determined. In the case of the returned questionnaires, information is missing about the educational level of the mothers for two subjects. In the control group, it was missing the results of five SDQ's. The Corsi Block was not administered to 10 children from the experimental group. In the instruments assessing inhibitory control, one child from the experimental group refused to perform conditions C and D of The Shape School Test, and one child from the control group did not meet the conditions necessary to perform the Go/No-Go EYT task. Additionally, due to human error, the total time of condition D of The Shape School Test of two control subjects was not properly recorded.

Results

Characteristics of the sample

The experimental group, consisting of 30 MPT children of whom 18 male, had a mean age of 66.20 months (SD 8.019). The control group, composed of 31 FT children, of whom 19 were male, had a mean age of 66.39 months (SD 6.407) (Table 1). Between the groups there were no differences in children's age ($t(59) = -0.101$; $p = 0.920$; $d = 0.026$; CI [−3.899; 3.525]), gender ($X^2(1) = 0.011$; $p = 1.000$; $\varphi = -0.013$; $N = 61$), or educational level of the mother ($X^2(6) = 11.138$; $p = 0.084$; Cramér's $V = 0.442$; $N = 57$) (Table 1). There were no differences in RCPM between MPT (M = 19.27; SD = 4.571) and FT group (M = 20.03; SD = 4.461) ($t(59) = -0.662$; $p = 0.511$; $d = -0.168$; CI [−3.080;1.548]). RCPM were corrected with Portuguese norms for children with ours sample sociodemographic characteristics.

It was verified that no child was wearing glasses or hearing aids at the time of data collection and that there were no complaints about these functions according to the parents or indications in the records of medical consultations. Within the experimental group, four pairs of twins were found, two of which were monozygotic. Also in the MPT group, one pair of twins had fetal-to-fetal transfusion syndrome, one child needed postnatal lung surgery, one child had a diagnosis of heart disease, and one child had a diagnosis of asthma. In all these cases, there were no associated complications and the performance of these children did not differ from the other MPT peers.

Working memory

The experimental group obtained lower scores in all instruments that assess working memory, statistically significant. MPT children evoked fewer number sequences in the direct digit span, manipulated fewer sequences in the backward digit, and also pointed out fewer blocks in Corsi in the direct direction and in Corsi in backward (Table 2).

Inhibitory control and cognitive flexibility

In The Shape School Test, discrete variables (correct inhibitions of condition B and correct inhibitions of condition D) were mostly concentrated on the maximum value, so we chose to dichotomize them in "all the correct answers" and "at least one wrong answer", and administer the Chi-square test. Initially, the data normality analysis verified the existence of extreme outliers that induced severe violations of the normality of the variables in both groups. Thus, we proceeded to eliminate eight outliers, two in the time variables of each

Table 2. Comparison of EF measures of MPT and FT.

Measure	Moderate preterm M (SD) [minimum; maximum]	Full term M (SD) [minimum; maximum]	*t*	*p*	*d*	CI
Digit Span Direct Order ($n_{MPT} = 30$; $n_{FT} = 31$)	4.10 (1.954) [0; 10]	5.26 (1.210) [4; 9]	−2.793	0.007	−0.714	[−1.988; −0.328]
Digit Span Backward Order ($n_{MPT} = 30$; $n_{FT} = 31$)	1.67 (1.729) [0; 6]	2.68 (1.301) [0; 6]	−2.586	0.012	−0.660	[−1.793; −0.229]
Corsi Direct Order ($n_{MPT} = 30$; $n_{FT} = 31$)	3.33 (1.709) [0; 6]	4.19 (1.515) [2; 7]	−2.082	0.042	−0.533	[−1.687; −0.034]
Corsi Backward Order ($n_{MPT} = 20$; $n_{FT} = 31$)	1.65 (1.927) [0; 7]	2.97 (1.494) [0; 7]	−2.743	0.008	−0.766	[−2.283; −0.352]
The Shape School Test:						
Condition A Time (sec) ($n_{MPT} = 28$; $n_{FT} = 31$)	21.32 (8.313) [11; 49]	22.23 (10.057) [12; 50]	−0.379	0.706	−0.099	[−5.756; 3.925]
Condition B Total Correct ($n_{MPT} = 30$; $n_{FT} = 31$)	14.33 (0.802) [12; 15]	14.65 (0.551) [13; 15]	−1.775	0.081	−0.465	[−0.663; 0.040]
Condition B Time (sec) ($n_{MPT} = 29$; $n_{FT} = 30$)	20.703 (8.278) [9; 47]	16.401 (4.915) [8; 29]	2.609	0.012	0.682	[1.232; 9.609]
Condition C Total Correct ($n_{MPT} = 29$; $n_{FT} = 31$)	13.34 (1.987) [8; 15]	14.26 (1.182) [11; 15]	−2.145	0.037	0.563	[−1.771; −560]
Condition C Time (sec) ($n_{MPT} = 29$; $n_{FT} = 29$)	48.36 (24.866) [20; 106]	37.12 (14.122) [19; 72]	2.118	0.040	0.130	[0.545; 21.944]
Condition D Total Correct ($n_{MPT\ o} = 29$; $n_{FT} = 31$)	13.34 (1.778) [9; 15]	13.61 (2.044) [7; 15]	−0.540	0.591	−0.141	[−1.261; 0.725]
Condition D Time (sec) ($n_{MPT} = 29$; $n_{FT} = 27$)	41.51 (22.656) [15; 96]	27.59 (10.747) [16; 56]	2.968	0.005	0.785	[4.443; 23.386]
Go/No-Go YET:						
Go Reaction Time (sec) ($n_{MPT} = 30$; $n_{FT} = 30$)	0.773(0.160) [0.51; 1.17]	0.764 (0.090) [0.64; 1.06]	0.245	0.807	0.069	[−0.059; 0.076]
No-Go Reaction Time (sec) ($n_{MPT} = 30$; $n_{FT} = 30$)	0.645 (0.091) [0.44; 0.83]	0.659 (0.116) [0.51; 0.98]	−0.890	0.377	−0.134	[−0.078; 0.030]
Go Accuracy ($n_{MPT} = 30$; $n_{FT} = 30$)	0.810 (0.162) [0.42; 1]	0.869 (0.125) [0.52; 1]	−1.594	0.116	−0.407	[−0.133; 0.015]
No-Go Accuracy ($n_{MPT} = 30$; $n_{FT} = 30$)	0.608 (0.232) [0.13; 0.93]	0.659 (0.194) [0.23; 0.93]	−0.930	0.356	−0.238	[−0.160; 0.059]
d' ($n_{MPT} = 30$; $n_{FT} = 30$)	1.443 (1.007) [−0.33; 4.15]	2.048 (0.920) [−0.09; 4.83]	−2.189	0.033	−0.627	[−1.026; −0.046]

Table 3. Comparison of correct inhibitions of The Shape School Test.

The shape school test	% Correct answers				
	Moderate preterm	Full term	X^2	*p*	φ
Condition B -Correct Inhibitions ($n_{MPT} = 30$; $n_{FT} = 31$)	66.7%	96.8%	9.350	0.003	−0.392
Condition D -Correct Inhibitions ($n_{MPT} = 29$; $n_{FT} = 31$)	76.7%	87.1%	0.654	0.500	−0.104

condition (A, B, C, and D). When evaluating the cases in question, a subject in the experimental group with two outliers was referred, in the observations, as unmotivated. The other extreme outliers were removed because they were not in line with the subjects' performance (Table 2).

In the analysis of the time of condition A, which could be an indicator of processing speed, no statistically significant differences were observed between groups (Table 2).

In Condition B, the experimental group did not obtain significantly different means in the total of named stimuli. However, the results indicate that, with statistical significance, the group of MPT infants took longer to perform the task, with a moderate dimension of the effect. In a more specific analysis, it was found that, in addition to taking longer to perform the task, MPT children also inhibited fewer stimuli (Table 3).

The variables extracted from the Go/No-Go EYT task met the requirements for the application of parametric statistics, (t-Student Test and the t-Student Test with Welch correction). Performance in the Go/No-Go had no significant differences in the mean reaction time of precision Go, nor in the mean reaction time of No-Go errors (Table 2).

In terms of precision, there were also no statistically significant differences in Go accuracy, nor in No-Go accuracy. However, the experimental group obtained a lower value in d' sensibility (MPT = 1.443; SD = 1.007; FT = 2.0480; SD = 0.920), with statistical significance, and a moderate effect dimension (Table 2).

Socioemotional development

The processing of the SDQ data was carried out based on a comparison of the total score of each subscale. Consecutively, the means of the SDQ subscales were compared with the t-Student Test (Table 4).

Regarding subscales Total of Difficulties, Conduct Problems and Hyperactivity and Inattention, parents characterized MPT children as having slightly fewer symptoms, with no statistical significance (Table 4).

In the Emotional Problems subscale, MPT children have more symptoms than the control group, with statistical significance.

Table 4. Comparison of SDQ subscales scores filled in by parents of MPT ($n = 27$) and FT ($n = 26$).

Subscale	Moderate preterm MD (SD)	Full term MD(SD)	t	p	d	CI
Total difficulties	12.15 (5.934)	13.81 (5.208)	−1.081	0.285	−0.297	[−4.743; 1.424]
Emotional Problems	3.52 (1.988)	2.27 (2.127)	2.210	0.032	0.607	[0.114; 2.384]
Conduct Problems	2.11 (1.888)	2.73 (1.823)	−1.215	0.230	−0.334	[−1.644; 0.404]
Hyperactivity Inattention	4.89 (2.342)	5.35 (1.468)	−0.855	0.397	−0.235	[−1.535; 0.621]
Peer Relationship Problems	1.63 (1.523)	3.50 (2.025)	−3.810	<0.001	−1.044	[−2.856; −0.885]
Prosocial Behavior	8.22 (1.423)	8.08 (1.647)	0.344	0.732	0.091	[−0.703; 0.993]

The results of Peer Relationship Problems subscale indicated that, in comparison with the control group, the experimental group presented fewer symptoms of difficulties in interaction with peers, with statistical significance.

In the subscale of Prosocial Behavior, there were no differences between groups.

Discussion

This study extends on previous research concerned with the impact of preterm birth. Particularly, we focused on the impact of moderate prematurity on EF of children between 4 and 6 years of age, comparing them with full-term peers. The descriptive analysis of the groups indicates that the paring of the subjects was well achieved.

Our results show that MPT children with average nonverbal intelligence quotient have lower performance in working memory tasks, inhibitory control and cognitive flexibility, and more emotional symptoms compared to their FT peers. The differences found between the groups do not seem to be attributable to the level of maternal education.

Relative to our main aim, statistical analysis confirms that MPT children of our study had more difficulties in verbal working memory, repeating and manipulating fewer sequences of digits. More precisely, the experimental group repeated and manipulated, on average, less one item than the control group. MPT children also showed a weaker performance in non-verbal working memory in comparison with their FT peers. In this context, our results are consistent with the literature that reports a worse working memory in MPT infants (Allotey et al., 2017; Caravale, Tozzi, Albino, & Vicari, 2005; Mulder et al., 2009; Vicari et al., 2004), since very early ages (Hodel et al., 2017; Johnson et al., 2015), which seems to be independent of the instruments used.

The performance of the experimental group in condition A of The Shape School Test suggests that, in MPT, processing speed is not the main mediator of performance in executive function measures, unlike what happens in more prematurely born children (Hodel et al., 2015, 2017). Regarding inhibitory control, in the condition B, MPT group had more difficulties inhibiting stimuli and took longer than the control group to perform the task, with a large effect magnitude (Cohen, 1988). Also, besides the percentage of correct inhibitions of condition D was not different between groups, MPT needed more time to perform the test. Although this task also implies cognitive flexibility, our results make us wonder if, in the case of MPT children, the possible structural changes may not strongly affect the accuracy of the answer, but rather the time needed to achieve an acceptable performance at the level of verbal inhibition.

Also in line with some results reported in the literature (Loe et al., 2019; Mulder et al., 2009), the MPT group showed a lower performance in visuomotor inhibition control. Although our study did not reveal significant differences in Go/No-Go task between the groups in reaction times and accuracy measures, when a measure of signal strength was calculated, the premature birth group showed a significantly lower d', indicating a lower capacity for target discrimination between noise. In this context, the non-application of SDT may lead to the erroneous conclusion that there were no differences between the groups performance when MPT children showed a lower sensitivity to inhibit a target stimulus whenever there was a dominant trend, a concern of authors such as Van der Kellen and collaborators (2008) and Wiebe, Sheffield, & Espy (2012) about neuropsychologic instruments. Wiebe and colleagues (2012) found that, in three-year-old FT children, No-Go time and accuracy are strongly correlated with the discrimination capacity of the stimulus, and the children who respond the fastest have a lower d' value. However, from the age of 3.75 years, children are expected to decrease reaction time and increase discriminatory capacity (Wiebe et al., 2012). This evidence leads us to question whether the worst performance observed in the inhibitory control of MPT children is a result of a persistent delay or an effective deficit in the maturation of the inhibitory control.

Consecutively, MPT also showed less verbal cognitive flexibility, with more difficulties alternating between different stimuli and requiring more time to complete the task. To our knowledge, there are no studies assessing MPT children of these ages with a measure of verbal cognitive flexibility, which makes it difficult to frame our results. However, cognitive flexibility strongly implies the contribution of working memory and inhibitory control (Diamond, 2013; Miyake et al., 2000), which are functions also affected in our sample.

Thus, at the level of socioemotional development, parents characterized MPT children with more emotional problems. However, in the subscale Peer Relationship Problems, the MPT group had a lower score. Considering the results of Emotional Problems, the result of the subscale of Peer Relationship Problems may not necessarily mean that the FT children show more difficulties of interaction at a pathological level, but rather that the MPT children have fewer problems of interaction with peers as a result of a poorer interaction. The assimilation of these results may indicate that the MPT children of our study are already more likely to have internalization symptoms that may be reflected in avoidance strategies and poor social interaction skills found in other studies (Allotey et al., 2017; Arpi & Ferrari, 2013;

Johnson et al., 2018), making them interact less with peers. These emotional difficulties may also be related to the difficulties in inhibitory control, since the literature has pointed out that this executive ability is an excellent predictor of social skills and internalization problems in preschool-age children (Hughes, White, Sharpen, & Dunn, 2000; Rhoades, Greenberg, & Domitrovich, 2009).

Contrary to what was expected, the differences found in the subscale of Hyperactivity Inattention were not significant. Given the existing studies, MPT children at school age with a diagnosis of ADHD have a predominant subtype of inattention, so conduct problems associated with this diagnosis are rarely observed (Johnson & Marlow, 2011; Wolke, 1998). Given the age of the group, school demands may not yet be enough for parents to find demarcated differences.

Therefore, in terms of neurobiological correlates, the deficits found in this study have been attributed, in the literature, to the adverse effects of premature birth on the developing brain, even in moderate prematurity and at low risk of medical complications (Cheong et al., 2016; Huppi et al., 1998; Inder, Warfield, Wang, Hüppi, & Volpe, 2005; Nagy et al., 2003; Ortinau & Neil, 2015; Tau & Peterson, 2010; Volpe, 2009).

As executive functions are crucial for school preparation (Blair, 2002; Ursache, Blair, & Raver, 2012; Willoughby, Magnus, Vernon-Feagans, & Blair, 2017) and for school skills such as arithmetic reasoning, reading, writing, reading comprehension, understanding instructions, and vocabulary development (Dehn, 2008; Hus, 2014; Prager, Sera, & Carlson, 2016), our data support the theory that these children, because are more likely to not being evaluated due to less medical monitoring, enter primary education at disadvantage compared to their FT peers (Van Baar, Vermaas, Knots, de Kleine, & Soons, 2009), which may explain the lower academic success of this population already described in the literature (Allotey et al., 2017; Chyi et al., 2008; Huddy et al., 2001; Quigley et al., 2012).

According to our analysis, the deficits reported in our study are associated with gestational age and not with the sociodemographic variables analyzed. However, it should be noted that, although there were no differences in the mother's level of education between the groups, a larger number of mothers in the term group had higher levels of education, which may influence the children's performance, since the literature highlights that maternal education may predict the quality of environmental stimulation (Ardila, Rosselli, Matute, & Guajardo, 2005; Greene, Patel, Meier, & Patra, 2016).

Therefore, the most important recommendation that can be drawn from this study is the importance of following-up MPT children since a very early age, to identify possible functional changes and promote a more targeted intervention, even in the preschool context, to overcome the difficulties of this population even before they enter primary school.

It may also be important to study whether the age of entry to preschool may influence the performance of MPT children in terms of EF and interaction with peers.

One of the strengths of this study was the pairing of subjects by age and gender, as well as the absence of differences between the mother's level of education. Also, the fact that we decided to include only children with a low risk of morbidity allows us to conclude that, despite a better neonatal path, with fewer health complications, MPT children continue at risk for the disruption of neural networks that translate into functional changes. A further strong point was the fact that we were able to assess an under-evaluated function – cognitive flexibility, evidencing its early development and how it is a vulnerable function in MPT preschoolers even in simple tasks. Finally, the use of standardized tests for the assessment of executive functions with questionnaires for the assessment of socioemotional development by parents prove to be an added value for a better understanding of the results obtained in relation to the existing literature.

However, our study also includes several limitations. The most important one was the non-application of the Corsi backward to all subjects of the experimental group, but only the direct direction, due to different protocols, which may or may not represent the visual working memory. This event requires us to be more cautious in interpreting the results obtained in this instrument. Similarly, the existence of four pairs of twins, two of which are monozygotic, may reduce the variability of the results in a modest sample such as ours. Another limitation relates to the nonuse of the WHO's categorization of prematurity, due to the subjects with low risk of morbidity we had available, as it contributes to an increase in the variability between studies on the subject. Also, the number and age of siblings of each subject, which affect EF and socioemotional development, should have been considered. Finally, the sample size, together with the non-inclusion of mild and severe neurodevelopmental changes, may hinder the generalization of results to the study population.

Nevertheless, it should be highlighted that our study reinforces the neuropsychological characterization of a poorly studied population (MPT) in a crucial age range for the development of the person, being one of the few studies to include the assessment of verbal cognitive flexibility and to emphasize the importance of using sensitivity measures in visual inhibitory control instruments, in order to avoid erroneous deductions.

Conclusion

This study showed that Portuguese children born between 31 and 33 weeks of gestational age show a pattern of deficits similar to the one described in several international studies, with difficulties in working memory, inhibitory control and emotional management, even in children who did not have serious medical complications. In fact, as these changes in the executive functions of MPT children may not be clinical, they are more easily overlooked in routine medical consultations, in daily life with parents and in preschool settings. Several studies, including ours, have reported deficits which may be correlated with the school difficulties that this population is more likely to have (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Allotey et al., 2017; Chyi et al., 2008; Huddy et al., 2001; Sylva, Melhuish, Sammons, Siraj-Blatchford, & Taggart, 2007).

The lack of assessment of executive functions in the preschool period and their consequent lack of intervention may be a missed opportunity, especially in moderate and late premature children. Evaluate and intervening even before functional deficits arise may help MPT in its cognitive and socioemotional development. It may also be important to identify efficient training programs and to develop contents that allows the stimulation of these children in an ecological manner and that cover children in disadvantaged contexts (Cardoso et al., 2016; Sasser, Bierman, Hienrichs & Nix, 2017; Walk, Evers, Quante & Hille, 2018).

In conclusion, if we compare our results with other studies with MPT infants, we find that there seems to be no safe gestational age that allows us to state that prematurity will not affect prefrontal lobe functions, even in cases of low risk of medical complications.

Disclosure statement

No potential conflict of interest was reported by the authors.

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