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## **Visuo-spatial perception in prematurely-born children without cerebral palsy or retinopathy but with scholar complaints**

### **Abstract:**

In absence of any complaints in early childhood, preterm children remain more at risk to encounter academic difficulties but their clinical picture remains not well characterized. We screened visuospatial perception in 70 children born preterm consulting for scholar complaints. Developmental Coordination Disorder (with or without comorbidities) was associated with high prevalence (27%) of impaired perception of spatial relationship. Prematurely-born children who obtained no diagnosis of Neuro-Developmental Disorder exhibited a high prevalence (31%) of impaired perception of object magnitude. Regression revealed that low gestational age and fetal growth restriction significantly predicted the magnitude but not the spatial relationship perception.

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## **Introduction**

Preterm birth increased about 15% between 1990 and 2010 (Blencowe et al., 2012; Vogel et al., 2018) with substantial decrease of mortality with the advances in neonatology (Demissie, 2001; Saigal & Doyle, 2008). This positive evolution is also seen in the decreasing prevalence of cerebral palsy (Sellier et al., 2016). Cerebral palsy in the context of preterm birth is generally linked to periventricular white matter damage in close proximity to dorsal stream and has been frequently associated with a characteristic high-level visuo-spatial processing impairment (Fazzi et al., 2004; Mazeau & Pouet, 2005). Preterm birth may also affect visual perception because of retinopathy of prematurity, or cerebral visual impairment which is another potential white matter sequela affecting the retrogeniculate visual pathway (Good, Jan, Burden, Skoczinski, & Candy 2001, Crotti et al. 2024a) with consequences on visual acuity, visual field and/or saccadic movements. In absence of any of these clinical signs in early childhood, there are some evidence children born pre-term still exhibit visuo-spatial processing impairment when tested at primary or secondary school age, especially in case of low Gestational Age (GA) and/or intra-uterine growth restriction (babies with Small birth weight for Gestational Age: SGA) (e.g., Gras et al., 2023; Perez-Roche et al., 2016). Even with no clinically detectable cerebral palsy, retinopathy or cerebral visual impairment, and with a clinical picture that does not either always reach the pathological thresholds of gold standard tests used to diagnose Neuro-Developmental Disorder (NDD), preterm children remain more at risk than their peers to encounter developmental and academic difficulties that may appear later (Arpino et al., 2010; Caravale, 2005; Perez-Roche et al., 2016; O'Reilly et al., 2020; Twilhaar et al., 2020).

Differences in microstructural brain organization have been reported even with no radiological signs of preterm brain injury in infants (Bouyssi-Kobar et al., 2018) and in adults (Vollmer et al., 2017) born preterm. As biological changes in white matter occur in the third

trimester of gestation, especially in the posterior tracts (Young et al., 2016), premature birth may cause invisible neural network dysmaturity hindering high-level visual processing. Accordingly, different neural networks are activated between young adults born at term and those born very prematurely during visual associating tasks (Narberhaus et al., 2009).

Behaviorally, differences in cognitive and motor development are measurable from 2.5 years old until adulthood (Cooke, 2003; Deforge et al., 2009; Hreinsdottir et al., 2013; Hutton et al., 1997; Perez-Roche et al., 2016; Sommerfelt et al., 1998). More precisely, very pre-term birth (<33 weeks of amenorrhea, with or without cerebral palsy) has been associated with impairment, at 5 years of age, in cognitive tasks involving simultaneous visual processing (simultaneous processing scale of the K-ABC, Larroque et al., 2008), which is consistent with dorsal stream (Valdois et al., 2019) vulnerability (Santos et al., 2009; Taylor et al., 2009). The dorsal visual stream underlies Elementary Visuo-Spatial Perception (EVSP) which consists in evaluating, through vision, the magnitude of objects (i.e. Length and Size comparison), as well as the relative position and orientation of objects' elements (i.e. the comparison of spatial relationships within multi-element geometrical shapes like comparison of Angle and of Dots' positions within a frame, or midline judgement (Landmark tasks) (Pisella et al., 2013). These elementary processes respectively rely on the middle occipital gyri as suggested by patients with hemi-micropsia (Cohen, Gray, Meyrignac, Dehaene, & Degos, 1994; Frassinetti, Nichelli, & di Pellegrino, 1999; Faillenot et al., 1999; Gandini, Lemaire, Anton, & Nazarian, 2008), and on the posterior parietal cortex as suggested by patients with Balint syndrome (Fink et al., 2000; McIntosh et al., 2002; Mishkin & Ungerleider, 1982a; Pisella et al., 2013). Several studies have highlighted a visuo-spatial deficit in preterm children using tests involving motor skills like copying (Caravale, 2005; Santos et al., 2009) and visuo-constructive (Caravale, 2005; Deforge et al., 2009; Hreinsdottir et al., 2013; Hutton et al., 1997; Sommerfelt et al., 1998) tasks. The EVSP screening test is

more specific because it is non-motor and relies on simple comparison judgements of geometrical shapes (Pisella et al., 2013, 2020, 2021). Its construct validity included significant correlation with subtests of the Wechsler Intelligence Scale IV relying on visuo-spatial analysis (Coding, Symbol search, Matrix Reasoning, Block Design), but not with Verbal Comprehension Index (Pisella et al. 2020).

The contribution of EVSP to the development of other cognitive and visuo-motor functions was reinforced by a study in which the EVSP screening test was administered in a population of term-born children (aged between 4 and 17) diagnosed with NDD (Pisella et al., 2021). EVSP performance was fragile (below the normal interquartile range) in more than half of children diagnosed with Developmental Coordination Disorder (DCD) or Specific Learning Disorder (SLD) and one third of children with DCD displayed EVSP performance below the outlier limit (OL), especially due to pathological scores in the Landmark tasks (subtests evaluating spatial relationships). EVSP performance did not differ from typically developing children for the groups of children diagnosed with isolated Language Disorder (LD) or Attention Deficit with or without Hyperactivity Disorder (AD/HD). To enable direct comparison with the population term born (Pisella et al., 2021), we used the same EVSP screening test in the present study involving children born preterm with no cerebral palsy, no retinopathy and no cerebral visual impairment, consulting for a potential NDD. Based on Gras et al.'s (2023) findings, we hypothesized that individuals born prematurely and with NDD would display higher prevalence of and more severe visuospatial deficits. Since high prevalence of EVSP deficit has been observed in NDD population (Pisella et al 2021), we hypothesized that the pre-term children impaired in EVSP would be the ones diagnosed with NDD. Finally, we wondered whether pre-term children display a peculiar profile of visuo-spatial deficit, and whether the Magnitude or the Landmark score of the EVSP screening test would be more related to the prematurity criteria.

## Materials and Methods

### *Study population*

For this retrospective study, we analyzed the EVSP screening test performance of 70 children born with less than 37 weeks of amenorrhea (gestational age, GA). Exclusion criteria were cerebral palsy, retinopathy of prematurity and known cerebral visual impairment, intellectual deficiency (Wechsler Intelligence Scale (WISC IV) mean score (IQ) lower than 70) or neurological lesions (figure 1). Children were excluded from the sample if they had abnormal Magnetic Resonance Imaging (MRI), Electroencephalogram (EEG) or transfontanellar ultrasound echography (ETF) reported based on clinical observations (without quantitative measures). The sample was mostly composed of patients addressed by private health professionals in charge of children's rehabilitation in the context of scholar complaints, and sometimes by neonatology departments. They came for out-patient consultation in our pediatric rehabilitation unit between 2012 and 2020 for a potential diagnosis of NDD. They underwent the EVSP screening test as part of their clinical exploration with approval of the Research Ethic Boards of the University Hospital (CPP Sud-Est II, number 2015- 54-2). The EVSP performance was not used to establish the diagnosis of NDD, which was defined through comprehensive evaluation by an interdisciplinary clinical team according to the DSM 5<sup>th</sup> (*Diagnostic and statistical manual of mental disorders: DSM-5 , 5th ed., 2013*) criteria and classifications. Validated tests were used, e.g. the NEPSY-II (Korkman et al., 2012), the M-ABC-2 (Marquet-Doléac et al., 2016), the Wechsler Intelligence Scale for Children (Wechsler, 2005, Wechsler, 2016), standard French oral and reading tests, TEDI-MATH (Van Nieuwenhoven et al., 2001), TEA-CH (Manly et al., 2006).

### *The EVSP screening test*

The EVSP screening test (Pisella et al., 2013) aims at evaluating visuo-spatial perception ability in isolation from any complex language, manual dexterity or visual gnosis. It is a simple paper test including 6 subtests (T1: Length comparison, T2: Size comparison, T3: Angle comparison, T4: Midline judgement, T5: Relative position comparison and T6: Position selection), fast to administer since it lasts maximum 15 minutes.

Pisella et al (2013) proposed to compute the sum of all the subtests, here labeled the Total Score, and also to distinguish two functional scores based on the neurotypical developmental trajectories: 1) the sum of the scores on Length (T1) and Size (T2) comparison subtests that reach their plateau of performance at 6 years old and 2) the sum of the scores on the four subtests requiring spatial integration between an object and a landmark (T3, T4, T5, T6) that do not reach their plateau before adolescence. They are labeled Magnitude and Landmark scores, respectively, in the present study. In line with the literature (Cohen, Gray, Meyrignac, Dehaene, & Degos, 1994; Frassinetti, Nichelli, & di Pelligrino, 1999; Gandini, Lemaire, Anton, & Nazarian, 2008; Faillenot et al., 1999; Fink et al., 2000; McIntosh et al., 2002; Mishkin & Ungerleider, 1982b), the performance of two patients with slightly different occipito-parietal damage reported in the Pisella et al (2013) study indicated that the distinction between these two scores may also be anatomical: the lesion of both patients involved the posterior parietal cortex and they failed in the Landmark tasks, while only the patient whose lesion also involved the left middle occipital gyrus failed the two Magnitude tasks.

Note that the internal consistency of the screening test was good, with Cronbach alpha = 0.758, indicating that inter-correlation between items was high but not too close to 1, i.e. that the test measures a unique function without redundancy (Pisella et al 2020). This also justifies to look at each subtest separately. Normative values are therefore provided for each subtest and for the magnitude and the landmark scores on Table 1.

*Testing conditions:*

The children were comfortably seated in front of a table on which the visual stimuli were presented in turn on cardboard sheets without any time constraints. Each subtest began with two easy training trials for which the experimenter gave the correct responses.

### *Scoring:*

As stated by Pisella et al. (2013, 2020) the raw scores (at each subtest, magnitude, landmark and total scores) depend on age (means increase and standard errors decrease with age). Instead, the raw score of an individual was therefore categorized into 6 scoring classes by comparison to the age-normative values. A raw score below the inferior outlier limit ( $OL = Q1 - 1.5 \times \text{interquartile range}$ ) corresponded to class 1. A raw score between the inferior outlier limit and the inferior limit of the interquartile range ( $Q1$ ) corresponded to class 2. A raw score between  $Q1$  and the median corresponded to class 3. A raw score between the median and the upper limit of the interquartile range ( $Q3$ ) corresponded to class 4. A raw score between  $Q3$  and the superior outlier limit ( $OL_{sup} = Q3 + 1.5 \times \text{interquartile range}$ ) corresponded to class 5. A raw score above the superior outlier limit corresponded to class 6. At any age, performance scored  $<Q1$  is considered fragile (corresponding to the lowest 25% scores of the age-matched neurotypical population) and performance scored  $<OL$  is considered pathological (corresponding to the lowest 5% scores of the age-matched neurotypical population).

### *Statistics*

#### *Prevalence of EVSP disorder*

Prevalence was established on the total score of the EVSP test, but also on the magnitude and landmark sub-scores, and on each subtest separately, in the total sample and in the different groups of gestational age ( $<$  or  $\geq$  33 weeks of amenorrhea, according to Larroque et al. 2008) and of NDD diagnosis (see Table 2).

In order to evaluate the prevalence of EVSP deficit in a specific group, we computed the number of individuals in this group who performed with a score inferior to  $OL$  and transformed it into an observed percentage that we compared statistically to 5% using a one-sided Fisher exact test.



To determine whether the occurrence of fragile EVSP scores was frequent in a specific group, we also computed the number of individuals who performed with a score inferior to Q1 and performed a one-sided statistical comparison to 25% using the Fisher exact test.

#### *Link between EVSP and prematurity criteria*

Since birth weight and gestational age (GA) are dependent variables, we classified each of the 66 children, whose birth weight was available, into 6 percentiles categories of fetal growth (FG) based on the normative curve of Yudkin et al. (1987). This FG categorical factor corresponds to where the child weight of birth is positioned compared to the weight of birth expected by its GA in a referenced population. A low percentile (<10<sup>th</sup> centile) indicates that the child is “Small for Gestational Age” (SGA) and therefore probably suffered from intra-uterine growth restriction (Perez-Roche et al. 2016). Children categorized above the 10<sup>th</sup> percentile are considered of “Appropriate growth for Gestational Age” (AGA). We then conducted simple and multiple linear regression analyses using Statistica 13.2 software (StatSoft, Inc) with GA and FG as independent and potentially complementary factors to explain the EVSP performance of preterm children.

#### **Results**

Our clinical sample is composed of 74% of boys, 82% lived in an urban area and 66% lived with their two parents. Children were aged between 6 and 15 years when they came to our clinical unit. They were born between 25 and 36 weeks of amenorrhea (gestational age, GA). The weight at birth was available for only 66 children, it ranged between 600 and 3270g.

In our sample of 70 preterm children (Figure 1), the prevalence of deficit (27%) and of fragile performance (54%) at the EVSP screening test were significant: percentages of children scoring as outlier (27% <OL,  $p < 0.001$ ) and scoring below the interquartile range (54% <Q1,  $p = 0.005$ ) were far higher than the theoretical percentages of 5% and 25%,

respectively. The visuo-spatial profile of this population differed to that of the normative population on both the magnitude and the landmark scores, with a significant prevalence of pathological performance on Length (T1:17%;  $p=0.011$ ), Angle (T3:15%;  $p=0.015$ ), Midline (T4:17%;  $p=0.011$ ) and Position selection (T6:28%;  $p=0.001$ ) subtests (figure 2).

### *Prevalence of NDD in the whole prematurely-born population*

Table 2 shows the distribution of NDD diagnoses established from the interdisciplinary assessments in our total sample and also by age category. We note that 81% of prematurely-born children consulting for a suspected learning disability had a confirmed diagnosis of Developmental Coordination Disorder (DCD), Attention Deficit with or without Hyperactivity Disorder (AD/HD), Specific Learning Disorder (SLD) and/or Language Disorder (LD). The most common NDD was DCD with a total prevalence of 53% ( $n=37$ ) in our sample, including 26 % displaying DCD without comorbidity ( $n=18$ ) and 27% displaying DCD with comorbidities ( $n=19$ , labelled “DCD+com” on figures 3 and 4, group consisting of  $n=7$  DCD+AD/HD,  $n=7$  DCD+AD/HD+SLD,  $n=4$  DCD+SLD+LD and  $n=1$  DCD+AD/HD+SLD+LD). The second most frequent NDD diagnosis was AD/HD ( $n=12$ ) with a prevalence of 17%.

### *Prevalence of EVSP disorder by NDD*

We first investigated the prevalence of EVSP disorder based on the observed total scores as a function of NDD diagnosis (figure 3).

The group of DCD had a significant prevalence of EVSP deficit (22% scored as outliers which was highly significant,  $p=0.02$ ) and 50% of these children had a total score below the normal interquartile range (Q1), percentage that did not reach significance ( $p=0.06$ ). In the group of children diagnosed with DCD and comorbidities (DCD+com), 47% scored as outliers ( $p<0.001$ ) and 74% scored below Q1 ( $p=0.006$ ).

In contrast, prevalence of EVSP disorder was not significant in AD/HD children, 33% scored below Q1 ( $p=0.25$ ) and only 8% scored below OL ( $p=0.35$ ).

None of the children of the LD group performed below Q1. Among the 3 children with SLD, 2 scored below OL and all scored below Q1.

Among the consulting children, 13 of them (19%) did not obtain any NDD diagnosis. Nevertheless, 7 scored below Q1 (62%,  $p=0.04$ ) and 4 scored as outliers (23%,  $p=0.03$ ).

When focusing on magnitude and landmark sub-scores (Figure 4), markedly different visuo-spatial profiles were observed between children with DCD and children without NDD. The DCD and DCD+com groups had similar and significant percentage of children performing as outlier on the landmark score (28%;  $p=0.008$  and 26%;  $p=0.009$ , respectively), and the DCD+com group additionally exhibited poor performance on the magnitude score (58% scoring below Q1  $p=0.04$ ). Conversely, the magnitude score was outlier for 31% of prematurely-born children who were not diagnosed with NDD ( $p=0.01$ ), and more than 50% of these children exhibited performance below Q1 on both landmark and magnitude scores ( $p=0.07$ ).

### *Link between EVSP and prematurity criteria*

In terms of fragility, the ratio of children scoring below Q1 for children born <33 weeks of GA was significant (67%;  $p=0.001$ ) while it was not for those born  $\geq 33$  weeks of GA (39%;  $p=0.15$ ). In contrast, the prevalence of EVSP deficit was similar in the two groups: the percentage of children scoring as outliers was 28% ( $p=0.001$ ) in the group born <33 weeks of GA and 26% ( $p=0.003$ ) in the group born  $\geq 33$  weeks of GA.

Similar results were obtained for FG, 63% of the 19 children of the SGA group = scored below Q1 ( $p=0.015$ ) while 49% of the 47 children with AGA scored below Q1 ( $p=0.02$ ), but the two groups showed the same prevalence of EVSP deficit (26% scored below OL ( $p=0.008$ ) in the SGA group and 28% ( $p<0.001$ ) in the AGA group).

The results of the simple and multiple regression analyses conducted to examine the relation between the prematurity criteria and the EVSP scores are presented on Table 3.

The results of simple and multiple regressions revealed that GA and FG were significant predictors of the magnitude score. GA predicted 11% of its variability ( $\beta=0.29$ ;  $p=0.01$ ) and FG 7% of it ( $\beta=0.26$ ;  $p=0.039$ ). The best model was obtained by the combination of GA and FG factors which explained about 15% of the magnitude score ( $R=0.39$ ). These relationships in fact concerned the subtest T1 evaluating length comparison, the combination of GA and FG also explained about 14% of it. GA was significantly related to the subtest T1 score ( $\beta=0.30$ ;  $p=0.01$ ) as well as FG ( $\beta=0.26$ ;  $p=0.01$ ), while neither GA ( $p=0.70$ ) nor FG ( $p=0.16$ ) was a significant predictor of the subtest T2 score evaluating size comparison.

In contrast, FG was not a significant predictor of the landmark score ( $\beta=-0.17$ ;  $p=0.20$ ) and GA did not reach significance ( $\beta=0.23$ ;  $p=0.07$ ). The model combining GA and FG explained only 6.5% of the landmark score of the population ( $p=0.14$ ).

As a result, GA did not reach significance as a predictor of the total score of the EVSP screening test ( $\beta=0.21$ ;  $p=0.075$ ) in simple regression analyses and FG was not a good predictor ( $\beta=0.05$ ;  $p=0.69$ ). In the multiple regression analysis GA almost reached significance ( $\beta=0.24$ ;  $p=0.056$ ) but the model combining GA and FG was not better ( $p=0.15$ ,  $R^2=6\%$ ).

## **Discussion**

This study concerned 70 prematurely-born children without cerebral palsy referred to the pediatric rehabilitation unit for suspected NDD. We retrospectively analyzed their performance at the EVSP screening test (Pisella et al., 2013, 2020, 2021) in order to evaluate their prevalence and profile of perceptual deficit 1) in relation with NDD diagnosis, compared to children with NDD born at term assessed in a previous study with the same screening test (Pisella et al. 2021), and 2) in relation with prematurity criteria. Among the children diagnosed with NDD, 37 displayed DCD (alone or associated with comorbidities like SLD) and this was associated with a high prevalence of EVSP deficit, 27% of them scoring as outliers for the perception of spatial relations (landmark score). This profile and prevalence are nevertheless similar to those observed previously in the children with DCD born at term (Pisella et al., 2021). Moreover, the landmark score did not depend significantly from the prematurity criteria. Only the magnitude score of the EVSP screening test, and especially the score of length comparison (T1), was significantly related to GA and FG, and this score was specifically failed in the group of preterm children who did not obtain any NDD diagnosis.

We will first discuss the type and frequency of NDD diagnosed in our sample and their profile of EVSP performance.

The most common NDD in the general prematurely-born population without cerebral palsy is DCD with a frequency varying between 9,5% and 51% across the studies (Arpino et al., 2010). This range depends on prematurity criteria, test and threshold applied for the evaluation, and most studies do not indicate whether DCD was associated with another NDD. Here, in our sample of 70 preterm children, 26% exhibited DCD in isolation of other NDD (18 children). The frequency of DCD doubled (53% corresponding to 37 children) when children with DCD and comorbidities are included, which matches the highest frequency found by Arpino et al (2010). In our previous study involving children with NDD born at term (Pisella et al., 2021) the prevalence of EVSP deficit was the highest for children exhibiting DCD, with 22% of the children impaired in the group with DCD only and 43% in the group with DCD and comorbidities. This deficit was driven by the landmark score which evaluates the visual perception of spatial relationships relying on the posterior parietal cortex. The question here was whether the children born pre-term and exhibiting DCD have a similar EVSP prevalence and profile than those born at term. The EVSP deficit concerned 22% of our population born prematurely and diagnosed with DCD and reached 47% when DCD was associated with other NDD (DCD+com group on figure 3). This deficit was driven by the landmark score even if the magnitude score was also fragile in children with DCD and comorbidities (DCD+com group on figure 4). This prevalence and profile are thus fairly comparable to what was observed previously in the population born at term (Pisella et al., 2021). This is in accordance with another study (Barray et al., 2008) that showed similar performance for DCD children whether or not diagnosed in the context of prematurity when evaluated with the NEPSY test.

The second most frequent NDD diagnosed in our sample was AD/HD with a frequency of 17% (12 children) consistent with the range between 15,7% and 20% observed in prematurely-born population across studies (Bhutta et al., 2002). Note that if we add the

pool of 15 children exhibiting AH/HD in the context of comorbidities (classified in the group of DCD+com which included n=7 DCD+AD/HD, n=7 DCD+AD/HD+SLD, n=4 DCD+SLD+LD and n=1 DCD+AD/HD+SLD+LD) the frequency of AD/HD in our sample reaches 38% (27 children) which exceeds the range reported by Bhutta et al (2002). The literature reports that the risk to develop AD/HD is higher for prematurely-born children (Walch, 2012) and it can be predictive for scholar difficulties (Jaekel et al., 2013; Olsén et al., 1998). In our sample of prematurely-born children, AD/HD was not associated with a significant prevalence of EVSP deficit or low scoring, a result similar to what was observed for AD/HD children born at term in our previous study (Pisella et al., 2021).

The diagnosis of developmental dyscalculia and dyslexia is not reported higher than in general population considering clinical criteria and thresholds (Bos & Tijms, 2012; Jaekel & Wolke, 2014). Nonetheless, many studies found that at group level preterm birth is associated with worse performance in reading, spelling and arithmetic (Holsti et al., 2002; Kovachy et al., 2015; Olsén et al., 1998; Perez-Roche et al., 2016; Twilhaar et al., 2018) due to specific patterns of visual- perceptual deficits (Perez-Roche et al., 2016). In our sample only 3 children exhibited SLD in isolation and two of them presented pathological EVSP scores. With the limitation that this represents a very small sample, this leads to the highest percentage of prevalence of EVSP deficit (Figure 3). If we add the pool of children exhibiting SLD and DCD classified in the group of DCD+com, the frequency of SLD reaches 21 % of the sample (15 children) with a high prevalence of EVSP deficit which stands in contrast with the fragile but rarely pathological performance of children with SLD born at term observed in the study of Pisella et al (2021). This would be consistent with the dorsal stream vulnerability of prematurely-born children which could affect geometry and written arithmetics as well as reading. Indeed, children born preterm are more impaired than term-born children in copying complex spatial configurations (Santos et al. 2009) and are more at risk to develop the visuo-

attentional type of dyslexia (Muneaux & Ducrot, 2014) which is also characterized by a deficit of simultaneous visual perception and of visual processing of spatial configurations (Valdois et al., 2004; Vialatte et al. 2023).

Finally, none of the pre-term children of our sample exhibited LD in isolation and only 5 children exhibited LD in the group with DCD and comorbidities. This confirms that LD is not linked to EVSP and reinforces the specificity of the link between parietal visuo-spatial dysfunction and a peculiar profile of DCD and/or SLD with high frequency of comorbidity. This is consistent with the contribution of the visual dorsal stream in both action and perception (review in Pisella et al 2009). On the one hand, one can speculate that the visual perception of spatial relationships is crucial for manual dexterity and can therefore contribute to movement coordination disorder. Indeed, in many tasks, movements are planned and controlled on-line based on the spatial relationships between the visual targets and landmarks, and the hand, or the active part of the tool hold by the hand, all seen in the workspace. For examples, to connect visual dots with a pen, to trace a line within the visual path of a labyrinth, or to copy a figure with the aim of precisely matching its size, orientation and spatial configuration, the visual position of the tip of the pen must be continuously compared to the other visual positions of the workspace (target, landmark or model) for the accurate guidance of the orientation and the length of each stroke. On the other hand, one can speculate that the ability to process the spatial combination of stroke specific of a written symbol, and the relative position of letters and numbers, is crucial for the recognition of words and numbers, and for apprehending the orders and alignments in written texts and mathematical operations.

Since similar conclusion was drawn based on our assessment of term-born children with NDD (Pisella et al 2021), one can wonder whether the dorsal-stream vulnerability is



linked to DCD and/or SLD, or even to cerebral palsy (see Ego et al. 2015; Crotti et al 2024a,b), rather than to prematurity. The second aim of the present study was therefore to explore the link between EVSP and prematurity criteria in the whole sample of 70 prematurely born children.

Prematurity and low birth weight are known risk factors for suboptimal neurodevelopment (Perez-Roche et al. 2016). However, birth weight is dependent on GA, unlike FG. Probably due to intra-uterine growth restriction (FG<10<sup>th</sup> centile) linked to placental insufficiency, full-term babies born SGA have also been reported to have lower neurodevelopment scores compared to normal-sized infants (Levine et al., 2015). We therefore included GA and FG as independent and potentially complementary predictors of EVSP performance. Note, however, that since fetal growth restriction is an important reason for premature delivery, these two factors remain difficult to disentangle in our sample. Perez-Roche et al (2016) studied these two factors as independent dimensions in children born preterm and full term, and could establish that both GA and being born SGA increase the risk of visual cognitive difficulties in school age children, with different corresponding patterns of deficiency. GA was associated with diminished visual-motor integration and figure-ground ability (handling of complex visual scenes), possibly reflecting dorsal white matter microstructural abnormality, especially of parieto-frontal tracts. SGA (whether born preterm or not) was not only associated with diminished visual-motor integration and figure-ground ability, but also with other visual functions, such as visual memory, form constancy and closure, suggesting more diffuse injury to visual pathways, possibly involving both white and grey matter. In the present results, we observed that lower GA (<33 weeks of amenorrhea) and fetal growth restriction (<10<sup>th</sup> percentile) did not lead separately to higher prevalence of EVSP deficit but increased the prevalence of fragile perceptual performance. Regressions analyses indicated that GA was the only criterion possibly related to the total score of the

EVSP screening test and to the landmark score, without reaching significance, while both GA and FG were significant predictors of the magnitude score (especially its length comparison subtest). This can be discussed together with the specific profile of the children born prematurely and not diagnosed with NDD who exhibited a significant prevalence of EVSP deficit (23% of their total scores were outliers) mainly due to pathological magnitude score (31% were outliers). This is the only group of children exhibiting this profile among the children coming for out-patient consultation in our unit; which leads us to suggest that a high prevalence of deficit at the length comparison sub-test could be characteristic of prematurity criteria, independent of NDD.

Altogether, the results of the present study suggest that two profiles of visuo-spatial deficit can be distinguished in prematurely-born children coming for out-patient consultation. The first one corresponds to an impaired perception of visuo-spatial relationship, possibly based on dorsal parietal dysfunction, that can be predictive of DCD and/or SLD diagnosis but not specific to prematurity. The second one corresponds to impaired object magnitude perception, possibly based on occipital dysfunction, that is significantly linked to GA and FG. This latter profile is not associated with drastic global motor coordination impairment, attention, reading or arithmetic disability (no NDD diagnosis) but can nevertheless explain the acknowledged increased academic difficulties in the population of prematurely-born children without cerebral palsy (Arpino et al., 2010; Caravale, 2005; Perez-Roche et al. 2016; O'Reilly et al., 2020; Twilhaar et al., 2020).

Each EVSP subtest can also be interpreted separately. In the whole sample, the most deficient skill found was the perception of relative position in cluttered environment since 28% of our total sample of prematurely-born children scored below the 5th centile (i.e.

outlier) at this subtest (T6). This suggests a difficulty to inhibit visual distracting information or to select relevant information from visual background. We also found significant visual perception deficit for length, angle, midline and relative position. It would be interesting to provide specific training and/or more adequate learning environment for these visuo-spatial deficiencies that may delay scholar acquisitions. Note that marked visuo-spatial deficit has been related to poorest academic performance and prognosis in a group of children with DCD (Gras et al., 2023), reinforcing the need of early detection, possible with the EVSP screening test. Deficient visual processing of length in particular was more frequent and severe in the prematurely-born children with no NDD diagnosis. Such impairment seems disabling enough to lead families to consult, but not sufficient to reach the thresholds of standard NDD diagnosis tests and criteria. It could be important not only for geometry, gesture control or discrimination between visually similar letters (h vs n for example), but also to develop concepts of numerical quantities (Fischer & Shaki, 2014). Prematurity thus appears more as a factor which will decrease general academic performance independent on the presence of NDD. Unfortunately, these children with visual-perceptual deficit cannot take advantage from therapeutic and pedagogic intervention because they do not fall under the DSM 5<sup>th</sup> classification and do not either benefit from the follow-up of cerebral palsy.

Nowadays, children with cerebral palsy and children with NDD benefit from neuropsychological long-term follow up leading to efficient rehabilitative strategies to prevent additional learning and/or behavioral problems. The present results may indicate the need for a similar specific neuropsychological follow-up for prematurely-born children without cerebral palsy but exhibiting visual-perceptual deficit. Early diagnosis allows for early intervention that is more beneficial and sustainable over time (Twilhaar et al., 2018). This could be achieved by promoting the systematic use of the EVSP screening test which provides

normative values from 4-years old. Such possibility of early screening to detect the children eligible for early intervention would overcome the main limitation of our study which is a biased sample of preterm children consulting for scholar difficulties, hence not representative of the whole population with premature birth.

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## TABLE TITLES:

**Table 1 : Normative values provided by age categories of two years from 4 years old for each subtest of the EVSP screening test, for the total score and for the magnitude and the landmark scores.**

Inferior outlier limit (OL=  $Q1 - 1.5 \times$  interquartile range); inferior limit of the interquartile range (Q1); median (M); upper limit of the interquartile range (Q3); superior outlier limit (OLsup=  $Q3 + 1.5 \times$  interquartile range)

**Table 2 : Retrospective data collected for each child of the sample from their clinical folder.**

Missing data : 4 cases did only have the total EVSP score and not the details of the performance by subtest in their records, 4 other cases did not have their weight at birth. Wechsler Intelligence Scale (IQ) scores ; Verbal Comprehension Index (ICV) ; Perceptual Reasoning Index (IRP) ; Processing Speed Index (IVT) ; Working Memory Index (IMT) ; High Intellectual Potential ( HPI) ; Gestational Age (GA) ; Birth weight (BW) ; Fetal Growth (FG) centile range and class for the regression analyses ; Age group at testing (years) ; Elementary Visuo-Spatial Perception (EVSP) total score centile range and class for the regression analyses ; Class for the regression analyses corresponding to the Magnitude score of the EVSP screening test ; Class for the regression analyses corresponding to the Landmark (Spatial Relationship) score of the EVSP screening test ; Developmental Coordination Disorder (DCD) ; Attentional Deficit (AD) ; Hyperactivity Disorder (HD) ; Specific Learning Deficit (SLD) ; Language Disorder (LD) ; TransFontanellar ultrasound Echography (ETF) ; cerebral Magnetic Resonance Imagery (MRI) ; ElectroEncephaloGraphy (EEG).

**Table 3 : Results of regressions analyses between the EVSP scores and the prematurity criteria.**

Results of simple regressions (1) and multiple regression (2) with GA and FG factors for each of the 6 subtests (T1, T2, T3, T4, T5 and T6), the Magnitude and the Landmark sub-scores, and the total score of the EVSP screening test. Parameters (determination coefficient  $R^2$ , beta estimate and p-value) mentioned in bold in case of p value  $<0.05$ , in *Italic* in case of p value between 0.05 and 0.10.

## FIGURE LEGENDS:

**Figure 1 :** Flowchart of the present study involving the assessment of children prematurely-born coming for out-patient consultation. IQ: mean score at the Wechsler Intelligence Scale IV; NDD: Neuro-Developmental Disorder; DSM5: Diagnostic and Statistical Manual of mental disorders 5<sup>th</sup> edition; GA: Gestational Age; WA: weeks of amenorrhea; FG: Fetal Growth percentile; SGA: Small weight for Gestational Age; AGA: Appropriate weight for Gestational Age. EVSP: Elementary Visuo-Spatial Perception.

**Figure 2:** Percentage of children scoring as outlier (<OL, dark bars) or below interquartile range (<Q1, light bars) at the EVSP screening test in the whole population of patients prematurely-born for the total score, for each of the 6 subtests (T1: Length, T2: Size, T3: Angle, T4: Midline, T5: Position et T6: Position selection in cluttered multi-choice) and for the Magnitude and the Landmark scores. Statistical threshold was fixed to 5% and marked by one star, when p-value was below 0.01, this is mentioned by two stars.

**Figure 3:** Prevalence of EVSP disorder (Total score) in the whole population and for each NDD category (no NDD: group with no diagnosis obtained; DCD: Developmental Coordination Disorder; SLD: Specific Learning Disorder, LD: Language Disorder; AD/HD: Attention Deficit with or without Hyperactivity Disorder; DCD+com: group with DCD and other comorbid NDD diagnosis). Significant prevalence with Exact Fisher test is highlighted in bold. Statistical threshold was fixed to 5% and marked by one star, when p-value was below 0.01, this is mentioned by two stars.

**Figure 4:** Profile of EVSP disorder (Magnitude and Landmark scores) for each NDD category (no NDD: group with no diagnosis obtained; DCD: Developmental Coordination Disorder; SLD: Specific Learning Disorder, LD: Language Disorder; AD/HD: Attention Deficit with or without Hyperactivity Disorder; DCD+com: group with DCD and other comorbid NDD diagnosis). Statistical threshold was fixed to 5% and marked by one star, when p-value was below 0.01, this is mentioned by two stars.