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Title	Development of egocentric and allocentric spatial orientation abilities in children born preterm with very low birth weight
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Abstract

Background: very low birth weight preterm infants show neuropsychological alterations in functions such as memory or visuospatial skills, although certain related functions, such as spatial orientation, have not been studied. Objectives: to compare children born preterm and at term between the ages of 5 and 7 years on egocentric and allocentric spatial orientation, and relate their performance to visuospatial skills, behavior, memory in daily environments, and perinatal risk factors. Study design: observational cross-sectional study Subjects: 88 very low birth weight children born preterm and 59 controls. Outcome measures: IQ (RIST), visuospatial skills (NEPSY II: Route Finding and Geometric Puzzles), spatial orientation (Egocentric and Allocentric Spatial Memory Test - Children's Version), behavior (BASC questionnaire for parents), memory in everyday environments (ECM-Q questionnaire for parents), and perinatal risk factors (collected from medical records). Results: Children born preterm obtain significantly lower scores than controls on the RIST, Route Finding, and Allocentric Spatial Memory Tests. Although spatial orientation is related to other neuropsychological variables in both premature and control children, there is no meaningful association with behavior or daily memory in children born preterm. The perinatal risk factors that are associated the most with visuospatial and orientation problems are surgical procedures and peri- and intraventricular hemorrhages. Conclusions: Children born preterm with low birth weight present difficulties in their spatial orientation, and for this reason, we propose including these types of tasks in the usual neuropsychological evaluation.

Keywords	Preterm, spatial memory, spatial orientation, egocentric, allocentric, visuospatial skills.

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Highlights

· Children born preterm show difficulties in egocentric and allocentric orientation

· Neuropsychological impairment in premature children is higher at younger ages

· Visuospatial problems are related to surgery and brain hemorrhages in neonatal period

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Authorship contribution statement

Fernández-Baizán: acquisition of data, interpretation, and writing – original draft. Alcántara-Canabal: acquisition of data and reviewing. Solís: conceptualization of the study, analysis and review. Méndez: conceptualization of the study, interpretation, review, and editing.

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Objectives: to compare children born preterm and at term between the ages of 5 and 7 years on egocentric and allocentric spatial orientation, and relate their performance to visuospatial skills, behavior, memory in daily environments, and perinatal risk factors.

Study design: observational cross-sectional study

Subjects: 88 very low birth weight children born preterm and 59 controls.

Outcome measures: IQ (RIST), visuospatial skills (NEPSY II: Route Finding and Geometric Puzzles), spatial orientation (Egocentric and Allocentric Spatial Memory Test - Children's Version), behavior (BASC questionnaire for parents), memory in everyday environments (ECM-Q questionnaire for parents), and perinatal risk factors (collected from medical records).

Results: Children born preterm obtain significantly lower scores than controls on the RIST, Route Finding, and Allocentric Spatial Memory Tests. Although spatial orientation is related to other neuropsychological variables in both premature and control children, there is no meaningful association with behavior or daily memory in children born preterm. The perinatal risk factors that are associated the most with visuospatial and orientation problems are surgical procedures and peri- and intraventricular hemorrhages.

Conclusions: Children born preterm with low birth weight present difficulties in their spatial orientation, and for this reason, we propose including these types of tasks in the usual neuropsychological evaluation.

Keywords

Preterm; spatial memory; spatial orientation; egocentric; allocentric; visuospatial skills.

1. Introduction

Children who were born before 37 weeks of gestation, called preterm or premature, show a high risk of suffering developmental alterations derived from prematurity, especially those born with very low birth weight, i.e., under 1,500 grams [1]. Neurodevelopmental disorders are related to behavioral problems and neuropsychological impairment [2,3]. The cognitive processes that are usually found to be affected in preterm infants are executive functions [4], memory [5], and visuospatial abilities [6,7]. Visuospatial abilities are necessary to identify, integrate, and analyze visual forms, details, and structures, and understand two- and three-dimensional spatial relationships, allowing us to safely navigate through our environment by accurately judging direction and distance [8].

Spatial orientation is the ability to reach a target place by following a path while navigating through the environment [9]. It is a complex ability that relies on several neuropsychological abilities: perceiving sensorial and proprioceptive stimuli, memorizing our surrounding environment, and planning a route to reach a specific location [10]. Spatial orientation is supported by the use of two frames of reference. On the one hand, the egocentric framework involves taking one’s body as the reference center while monitoring movements, turns, and distances. On the other hand, the allocentric framework relies on environmental cues or landmarks and is independent from one’s point of view, allowing the development of mental maps as representations of the real world [11,12]. Egocentric and allocentric orientation show different courses of development during childhood. Whereas the egocentric framework is the first to emerge in infancy [13,14], the allocentric framework starts to be used with relative efficiency at two years of age [15]. This process ends when children are able to integrate and coordinate egocentric and allocentric information. According to the environmental knowledge acquisition model [16], children are first able to recognize landmarks, then combine egocentric information with consecutive landmarks, and, finally, memorize and organize landmarks within a mental map. Although there is a lack of agreement about when this process ends, it is generally considered to occur between the ages of 7 and 10 [17,18]. Likewise, boys have some advantage over girls in allocentric orientation [19,20], and, therefore, gender is a relevant factor to consider in spatial orientation assessments.

We currently know that preterm children show problems with spatial orientation-related abilities, such as visuospatial skills [6] and short-term and working memory [5,21,22]. However, it is still not clear whether preterm children present spatial orientation difficulties. It seems that preterm children at 7 and 8 years of age show difficulties when orienting themselves on a virtual task [23]. However, this methodology fails to examine the two frameworks separately. Although virtual tasks have a lot of advantages related to adapting the difficulty level, ease of application, and the possibility of combining them with neuroimaging techniques, they usually lack some sources of information that are present in daily life orientation, such as proprioceptive, vestibular, or optic flow stimuli [15,24]. Therefore, evaluation tasks that try to reproduce some of the natural conditions of spatial orientation, but in a controlled environment, could provide us with a more accurate measurement of spatial orientation performance in real contexts.

Moreover, in prematurity, it is important to consider other variables that may be related to spatial orientation performance. The presence of some behavioral difficulties, such as internalizing, externalizing, attention, hyperactivity, emotional problems, and social problems [2,3], could potentially affect cognitive performance [3], and some perinatal risks and maternal and newborn conditions can have a later impact on neurodevelopment. Visuoperceptual abilities in premature children may be associated with medical complications at birth [1]. However, this result was obtained using an index that measures perinatal risk and fails to differentiate which of these perinatal and obstetric variables influence later development.

The aim of the present study was to analyze the egocentric and allocentric spatial orientation performance in children born preterm with low birth weight, compared to typically developing children between 5 to 7 years old. Additionally, we aimed to discover whether the egocentric and allocentric frameworks develop at the ages of 5, 6, and 7, and whether spatial orientation performance is gender-related in both groups. We also aimed to explore the relationship between egocentric and allocentric spatial orientation performance and the development of other cognitive functions, such as visuospatial skills, as well as behavioral problems and spatial memory in daily contexts. Lastly, we aimed to evaluate the association between perinatal risk factors and later spatial orientation and visuospatial abilities in children born preterm with low birth weight.

2. Method

2.1. Participants

Preterm children were recruited from a cohort of neonates under 1,500 g and born before 37 weeks of gestation between January 2009 and December 2011 in the neonatal intensive care unit (NICU) of the Central University Hospital of Asturias (HUCA), Spain. Inclusion criteria included being between 5 and 7 years old at the time the study was carried out, a gestational age at birth of less than or equal to 37 weeks, and a birth weight of less than or equal to 1,500 g. Exclusion criteria were death, no follow-up, and preterm children with a birth weight of less than 1,500 g and with a diagnosis of malformations and/or congenial syndromes that led to evident neurological alterations. Control children born at term, also between 5 and 7 years old, were recruited from schools, primary care centers, and hospitals in Oviedo (Spain). Exclusion criteria included psychological, physical, or neurological conditions and disorders that could potentially interfere with the results, as well as an intelligence quotient (IQ) below 85, measured with the Reynolds Intellectual Screening Test (RIST) [25]. The final sample was composed of 88 preterm children and 59 control children. Parents of both groups were informed about the aims of the study and provided their written informed consent before the study began. The study was conducted in accordance with the Helsinki declaration for research in human subjects, and it was approved by the regional ethics committee.

2.2. Measurements

2.2.1. IQ

For IQ screening, we employed the *RIST* (*Reynolds Intellectual Screening Test*) [25], administered in 10 to 15 minutes and composed of two tasks; *Guess what* for verbal IQ assessment and *Odd-item* for non-verbal IQ assessment. In *Guess what*, the child has to find the correct word for each definition the examiner reads aloud, whereas in *Odd-item*, the child has to choose which picture does not match the rest of the pictures on the same page.

2.2.2. Visuospatial abilities

For the visuospatial abilities assessment, we employed two sub-tasks from the NEPSY-II battery [26]: *Geometric Puzzles* for mental rotation and *Route Finding* for directionality, spatial relations, and interpretation of schematic maps. On *Geometric Puzzles,* the child has to match two pairs of equal figures, but some figures could be rotated. On *Route Finding,* the child has to point out the house he/she would reach if he/she were to follow a certain path previously seen on a complex map, and follow this path with his/her finger.

2.2.3. Spatial orientation

For the spatial orientation assessment, we employed two tests: Egocentric and Allocentric Spatial Memory Tests [9,27], adapted to children (Fig. 1).

First, the Egocentric Spatial Memory Task consists of four opaque panels (180 x 180 cm.) surrounding a square template (90 x 90 cm.) that form a grid (nine small squares in a 3x3 disposition, 30x30 cm. each) placed on the floor. On the Egocentric Spatial Memory Task Part A, the child has to memorize the position of two cards (pictures of a sun and a car, measuring 15 x 15 cm. each) placed in two squares on the grid while he/she is standing in the central square of the template. After 10 seconds, the examiner removes the cards, and the child must return each picture to its position. On the Egocentric Spatial Memory Task Part B, the procedure is the same, but immediately after the examiner has removed the cards, the child is rotated (90º or 180º to the left or the right, as determined on the test), and then he/she is asked to put each picture in the same place as before. The panels avoid access to environmental landmarks, so that the child is forced to use a purely egocentric response. Each part, A and B, is composed of 5 consecutive trials. In each trial, cards are in a different position than the one previously memorized, and the child can score one point for each picture placed correctly. Thus, the child can score between 0 and 10 points on each part (Fig. 1.A).

Second, the Allocentric Spatial Memory Task consists of a circular template placed on the floor (65 cm. diameter), with eight squares (18x18 cm.) along the perimeter. Again, the child has to memorize the position of the two previous cards (pictures of sun and a car, measuring 15 x 15 cm. each) placed in two of the squares of the template while he/she is standing in front of the circle. After 10 seconds, the examiner removes the pictures and blindfolds the child, walking with him/her around the template to a different location. Then, the examiner removes the mask and asks the child to place both pictures in their correct location. Errors are immediately corrected by placing the cards in their right position. This task is composed of 3 blocks with 4 trials each. For each block, the position of the cards is the same throughout the 4 trials. The child receives one point for each picture placed correctly, so that the total score on this test varies between 0 and 24. This test includes a stop criterion: the task ends if the child obtains 0 points on two consecutive trials in the same block (Fig. 1.B).

Finally, parents completed an adapted version of *Evaluación Clinica de la Memoria (ECM-Q)*, using only 9 of its items [28], rated on a Likert scale from 1 to 4 (1 – Never, 4 – Always). Parents are asked about their child's spatial memory abilities in a daily context. The items included were: (1) He/she remembers the path to go home; (2) He/she has a good sense of direction; (3) He/she forgets how to get to a place unless he/she has been recently told how to reach it; (4) He/she remembers where he/she has left his/her things, (5) He/she gets lost in familiar places; (6) He/she remembers where things are kept; (7) He/she recognizes places that he/she has been to before; (8) He/she is used to getting lost in places where he/she has been before; and (9) He/she is good at learning the path to reach a new place.

2.2.4. Behavioral and emotional outcomes

Parents were also asked to complete the Behavior Assessment System for Children – Parent's version (BASC) [29]. Items varied from 130 to 134 depending on the test level: level 1 (3- to 6-year-olds and Preschool Education) and level 2 (6- to 12-year-olds and Primary Education). Each item is rated on a Likert scale with 4 levels (A: never; B: sometimes; C: frequently, and D: almost always). This questionnaire consists of an adaptive and adjustment dimension, as well as a clinical and maladaptive dimension. The adaptive dimension includes subscales of adaptability, social skills, and leadership behaviors, whereas the clinical dimension involves aggressiveness, hyperactivity, behavioral problems, attention problems, atypicality, depression, anxiety, shyness, and somatization behaviors.

2.2.5. Perinatal risk factors

The variables considered for analysis were related to prenatal and/or maternal conditions during pregnancy, neonatal and/or early postnatal treatments and interventions, diseases, and pathologies, and neurological alterations. Regarding the items related to prenatal and maternal conditions, we included in vitro fertilization (IVF), multiple or single pregnancy, vaginal or caesarean delivery, chorioamnionitis, maternal arterial hypertension (AHT), prescribed maternal corticoids, and prescribed maternal antibiotics. In terms of neonatal and early postnatal interventions and treatments, we analyzed intubation, continuous positive airway pressure, mechanical ventilation, surfactant, inotropic, and surgery procedures, which in our sample involved colostomy and ileostomy related to necrotizing enterocolitis and ventriculoperitoneal shunt for hydrocephalus. Diseases and pathologies included necrotizing enterocolitis (NEC), hyaline membrane disease (HMD), patent ductus arteriosus (PDA), apnea, transfused anemia, and sepsis. The neurological alterations registered were related to periventricular and intraventricular hemorrhage (from grades 0 to III) and periventricular leukomalacia. In terms of descriptive variables, we considered intrauterine growth status, APGAR at 1 and 5 minutes, and neurodevelopmental disorders. All variables were obtained retrospectively from electronic medical records.

2.3. Procedure

Children were assessed individually by trained psychologists in one session that lasted around 60 minutes. The procedure began with the Reynolds Intellectual Screening Test (RIST) and was followed by the Geometric Puzzles from NEPSY-II, Route Finding from NEPSY-II, Egocentric Spatial Memory Test – Children's version, and Allocentric Spatial Memory Test – Children's version. Parents completed sociodemographic, behavioral, and daily memory questionnaires. The experiment took place at the Faculty of Psychology and in primary schools and hospitals in Oviedo, Spain.

2.4. Statistics

All analyses were performed using SPSS 19.0 for Windows. Three-way ANOVA were employed to compare preterm and control neuropsychological performance (Group x Age x Gender). Maternal education was included as a covariate in these analyses. In order to control Egocentric part A performance, this variable was included as a covariate in a three-way ANOVA (Group x Age x Gender) in the Egocentric B analysis. When performance in each group separately was analyzed, two-way ANOVA (Age x Gender) were used. Repeated-measures ANOVA were carried out to explore differential performance across blocks of trials in the allocentric framework. A Pearson correlation was conducted to verify associations between variables. Finally, a Mann-Whitney U test was conducted when the number of participants in a group was large, as in the perinatal risk factor analysis. A p-value lower than 0.05 was considered significant.

3. Results

3.1. Sample characteristics

Table 1 shows the children's main sociodemographic characteristics. Table 2 presents neonatal and neurodevelopmental variables of the preterm sample. There are no significant differences between the groups in terms of gender or age (p>0.05), but there are significant differences in the level of maternal education (χ^2_3=-15.983; p=0.001; r=0.329), where control children's mothers show higher formal education. Therefore, the variable Maternal education was considered in the following analyses.

3.2. Spatial orientation, visuospatial abilities, and IQ assessment

The ANOVA analysis (ANOVA Group x Age x Gender x Maternal education) revealed statistically significant differences between preterm and control children on the RIST ($F_{1,123}$=39.168; p<0.001; η^2=0.240), Route Finding ($F_{1,123}$=6.804; p=0.010; η^2=0.052), Egocentric part A ($F_{1,123}$=16.180; p<0.001; η^2=0.116), Egocentric part B ($F_{1,123}$=7.182; p=0.008; η^2=0.055), Total Allocentric ($F_{1,123}$=23.407; p<0.001; η^2=0.160), Allocentric block 1 ($F_{1,123}$=6.200; p=0.014; η^2=0.048), Allocentric block 2 ($F_{1,123}$=20.026; p<0.001; η^2=0.140), and Allocentric block 3 ($F_{1,123}$=10.935; p=0.001; η^2=0.082) (Fig. 2.). However, when the effect of Egocentric Part A was controlled in the Egocentric B analysis, group differences in Ego B were no longer significant (p=0.197) (Table 3). In all these variables, the scores obtained were higher for the control group than for the experimental group. The descriptive statistics for the neuropsychological performance of both the preterm and control groups are shown in Table 3.

A repeated-measures ANOVA (Blocks x Age x Gender) of the performance on the different Allocentric blocks showed significant differences ($F_{2,81}$=7.767; p=0.001; η^2=0.161), although no significant results were associated with Age or Gender. These differences were found only in the preterm group. This group presented differences between blocks 1 and 2 (t_{86}=3.5; p=0.001), and between 1 and 3 (t_{86}=2.524; p=0.015), but not between 2 and 3 (p=0.493) (Fig. 2.). In the control group, no significant differences were found when comparing performance on Allocentric blocks 1, 2, and 3 (p=0.532) in a repeated-measures ANOVA (Blocks x Age x Gender).

According to the Age variable, analyzing the total sample, significant differences were found on Geometric Puzzles ($F_{2,123}$=45.648; p<0.001; η^2=0.426), Route Finding ($F_{2,123}$=7.851; p=0.001; η^2=0.113), Egocentric part B ($F_{2,123}$=3.130; p=0.047; η^2=0.048), Total Allocentric ($F_{1,123}$=5.925; p=0.003; η2=0.088), Allocentric block 2 ($F_{2,123}$=4.507; p=0.013; η^2=0.063), and Allocentric block 3 ($F_{2,123}$=4.979; p=0.008; η^2=0.075). The only significant Group x Age interaction was found on Allocentric block 1 ($F_{2,123}$=4.052; p=0.020; η^2=0.062), which revealed significant differences between the group of 5-year-olds and the group of 6-year-olds (p=0.022). Tukey's post-hoc analysis of Geometric Puzzles revealed significant differences between 5- and 6-year-olds (p=0.033), between 5- and 7-year-olds (p<0.001), and between 6- and 7-year-olds (p<0.001). On Route Finding, differences were found between 5- and 6-year-olds (p=0.049), 5- and 7-year-olds (p<0.001), and 6- and 7-year-olds (p=0.004). Egocentric test part B revealed significant differences only when comparing the 5-year-old group with the 7-year-old group (p=0.003). On the total Allocentric task scores, significant differences were found between 5- and 6-year-olds (p=0.001) and between 5- and 7-year-olds (p=0.001). In the second block of the Allocentric task, differences were also observed between 5- and 6-year-olds (p=0.042) and between 5- and 7-year-olds (p=0.003). The same situation is repeated in the third block of the Allocentric task, revealing differences between 5- and 6-year-olds (p=0.007) and between 5- and 7-year-olds (p=0.029). In all these comparisons, the older groups performed better than the younger ones. However, these age differences were found exclusively in the preterm sample. In the control sample, no significant differences were found through an Age x Gender ANOVA on Egocentric part A, B, Total Allocentric, or any of its blocks (p>0.05). The same ANOVA analysis for the preterm sample revealed statistically significant differences between ages on Egocentric part B ($F_{2,82}$=5.780; p=0.004; η^2=0.124), Total Allocentric ($F_{2,82}$=6.945; p=0.002; η2=0.145), Allocentric block 1 ($F_{2,82}$=8.265; p=0.001; η2=0.168), and Allocentric block 2 ($F_{2,82}$=4.485; p=0.014; η^2=0.099). Tukey's post-hoc analysis revealed differences on Egocentric part B between preterm 5- and 7-year-olds (p=0.002); on Total Allocentric, between preterm 5- and 6-year-olds (p=0.004) and between preterm 5- and 7-year-olds (p=0.005); in the first block of the Allocentric task, between preterm 5- and 6-year-olds (p=0.001), and in the second block, between preterm 5- and 7-year-olds (p=0.011). No significant differences were obtained for the Gender variable or the Age x Gender interaction.

None of the previous comparisons revealed significant differences based on Gender or Maternal education, or the interaction between these factors.

3.3. Relationships between egocentric and allocentric frames of reference and perinatal risk factors

Starting with the analysis of gestational age and birth weight, there were no statistically significant correlations between these two variables and Egocentric and Allocentric spatial orientation performance, visuospatial abilities, or IQ ($p>0.05$). Regarding the perinatal risk factor analysis, the preterm sample was separated into two groups, depending on whether that specific condition or treatment had been present or not. Thus, when separating children according to single or multiple births, significant differences were found on Total Allocentric ($U=445.5$; $p=0.007$; $d=0.328$), finding that those children born in single births scored better. Dividing preterm children by type of delivery, vaginal or caesarean section, statistically significant differences were observed on Route Finding ($U=615$; $p=0.040$, $d=0.507$), with better performance by children born with vaginal delivery. Regarding continuous positive airway pressure (CPAP), significant differences were found on Geometric Puzzles ($U=389$; $p=0.039$, $d=0.610$), where children who received CPAP scored worse than those that did not. For any type of surgical intervention, significant differences were found on the RIST ($U=112$; $p=0.026$; $d=0.974$), Geometric Puzzles ($U=122$; $p=0.040$; $d=0.979$), Route Finding ($U=100.5$; $p=0.014$; $d=1.180$), Egocentric part A ($U=93$; $p=0.009$; $d=1.320$), and Egocentric part B ($U=110$; $p=0.024$; $d=1.056$). In all these comparisons, children who had not undergone any surgery had better scores. Regarding the presence of necrotizing enterocolitis, there were significant differences on the RIST ($U=37$; $p=0.004$; $d=1.752$) and Egocentric part B ($U=47$; $p=0.012$; $d=1.421$), where children without necrotizing enterocolitis obtained better scores. In the case of late onset sepsis, significant differences appeared on Geometric Puzzles ($U=423$; $p=0.002$; $d=0.853$) and Route Finding ($U=434.5$; $p=0.004$; $d=0.731$), with children who received this diagnosis performing worse. Finally, when considering the presence of intra-periventricular hemorrhages to any degree, statistically significant differences were obtained on Geometric Puzzles ($U=372$; $p<0.001$; $d=1.118$), Route Finding ($U=522$; $p=0.015$; $d=0.775$), Egocentric part A ($U=461.5$; $p=0.006$; $d=0.824$), and Total Allocentric ($U=368.5$; $p<0.001$; $d=1.022$). When the degree of the hemorrhage was considered (0, I, II, or III), significant differences were found on Geometric Puzzles ($\chi^2_3=14.388$; $p=0.002$; $d=0.803$), Egocentric part A ($\chi^2_3=12.021$; $p=0.007$; $d=0.703$), and Total Allocentric ($\chi^2_3=16.910$; $p=0.001$; $d=0.904$). Comparing the degree, significant differences were only found between degrees 0 and I on Geometric Puzzles ($p=0.001$), Egocentric part A ($p=0.004$), and Total Allocentric ($p<0.001$). IVF, chorioamnionitis, AHT, corticoids, antibiotics, intubation, mechanical ventilation, surfactant, HMD, PDA, apnea, anemia, and periventricular leukomalacia did not show any significant differences.

3.4. Relationships between egocentric and allocentric frameworks and visuospatial functions, behavior, and memory in everyday contexts.

Starting with the associations for the neuropsychological measures (Table 4), in the preterm group, Egocentric part A was significantly related to the RIST ($r=0.435$; $p<0.001$), Geometric Puzzles ($r=0.470$; $p<0.001$), and Route Finding ($r=0.287$; $p<0.001$), with first and second correlations showing a low effect size and the third showing a very low effect size. Egocentric part B correlated significantly with the RIST ($r=0.230$; $p=0.032$), with a very low magnitude, and with Geometric Puzzles ($r=0.457$;

p<0.001) and Route Finding (r=0.397; p<0.001), both with a low magnitude. The total Allocentric test was significantly associated with the RIST (r=0.266; p=0.013), with a very low effect size, as well as with Geometric Puzzles (r=0.409; p<0.001) and Route Finding (r=0.466; p<0.001), in both cases with low effect sizes. Control children showed significant associations between Egocentric part A and the RIST (r=0.278; p=0.033) and Route Finding (r=0.274; p=0.038), both with a very low magnitude. Finally, Egocentric part B was significantly related to Route Finding (r=0.388; p=0.003), with a low effect size. All these correlations show direct relationships between these variables.

On the behavior analysis, in order to avoid the influence of age, T-scores for each variable were used instead of direct scores. Thus, in the preterm sample, only Leadership, assessed in 6- and 7-year-old children, but not 5-year-olds, correlated significantly and positively with Total Allocentric (r=0.354; p=0.012), with a low magnitude. In control children, Egocentric part A correlated significantly with Leadership (r=0.477; p=0.002), with a low magnitude, and with Adaptative abilities (r=0.280; p=0.033), with a very low magnitude. Egocentric part B was significantly and negatively associated with Atypicality (r=-0.294; p=0.025), with a very low effect size.

Finally, after analyzing spatial memory in everyday environments through the ECM-Q questionnaire, no significant correlations were revealed in the preterm sample. However, in control children, Egocentric part A was significantly and positively associated with Item 1 (r=0.399, p=0.018) and Item 7 (r=0.478, p<0.001), and significantly and negatively associated with Item 3 (r=-0.325, p=0.026), all with low magnitudes. The Allocentric test was significantly and directly related to Item 2 (r=0.379, p=0.007), Item 4 (r=0.287, p=0.043), and Item 9 (r=0.312, p=0.031), and significantly and inversely related to Item 8 (r-451=, p=0.001), with all these correlations showing a very low to low effect size.

4. Discussion

The aim of the present study was to investigate spatial orientation performance in children born preterm with a low birth weight, compared to a control group of children born at term. To our knowledge, this is the first study to employ relevant functional tasks to assess spatial orientation in preterm children, making it possible to analyze the orientation frameworks separately. We also aimed to investigate spatial orientation development at these ages [5 to 7] and relate their performance with other relevant factors, such as other cognitive abilities, behavior, memory in daily contexts, and perinatal risk factors.

First, we found that preterm children show neuropsychological difficulties in terms of IQ and visuospatial abilities, which are related to directionality and map interpretation. These results agree with previous studies, where children who were born prematurely tend to score lower on the intelligence test and seem to present visuospatial perception alterations [6,7]. Moreover, we also found that allocentric spatial orientation is impaired in this population. Previous studies conducted using virtual tasks and based on allocentric responses [23] support these results, with 7- and 8-year-old preterm children making more mistakes than their at-term peers. The hippocampus is one of the main regions altered in a preterm child’s brain, and it is also related to visuospatial memory problems [30]. Therefore, this hippocampal alteration could explain why preterm children show allocentric orientation difficulties. However, some other brain dysfunctions have been found to be associated with memory difficulties in preterm children [5,22]. It is also important to mention that IQ is the most discriminative measure between children born preterm and at term, followed by Allocentric and Egocentric part A Spatial Memory Tasks, indicating that their spatial orientation performance is even worse than their visuospatial abilities. It is necessary to consider that, although both are referred to as "Egocentric", Part A serves as a short-term visuospatial memory index in 3D environments and as a measure of reference memory, whereas Part B truly assesses the egocentric framework. Alterations in visuospatial memory have been found in preterm children throughout childhood [21,22].

Moreover, there are no differences between the scores on the allocentric blocks in the control sample, although we do find differences in the preterm group. This result indicates that there is no learning effect in the control sample. One possible explanation is that the performance from the first block of the task is already high and maintained throughout all the blocks. Greater difficulty on this task could allow us to find out whether this learning effect takes place. In preterm children, the differences in performance occur in the first block, compared to the others. Preterm performance does not have a clear learning curve, but the values descend in the second block and recover partially in the third. Therefore, we cannot conclude that these differences are due to learning problems. Other possible explanations could have to do with the fatigue factor, given that this task was the last one in the assessment protocol. Additionally, neuropsychological functions that have been found to be altered in preterm children, such as attention and working memory [22], could be influencing these results: attention levels could decrease as the task progresses, and working memory problems could cause previously learned trials to interfere in the performance on the newer ones. Another possible factor would be the lack of motivation, especially in those children who made more errors.

Regarding the age of the participants, younger children tend to score lower than their older peers on visuospatial functioning and egocentric and allocentric spatial performance. Whereas visuospatial tests (Route Finding and Geometric Puzzles) discriminate between all ages, the Allocentric test differentiates the 5-year-old group from the rest of the age groups, and Egocentric test part B differentiates between 5- and 7-year-olds. However, it seems that the only difference between preterm and control performance related to age is in Block 1 of the Allocentric test, specifically, between 5- and 6-year-old children. Thus, premature birth seems to be the relevant factor.

Regarding gender, boys do not outperform girls and vice versa, in preterm or at-term children, on spatial orientation performance. On spatial orientation virtual tasks, typically developing males [20] and preterm males [23] seem to perform better than girls. However, on real-based tasks, results are still contradictory in children born at term, with some studies finding that boys outperform girls [19,31], whereas others do not observe any differences based on gender [32], or they even reveal that girls achieve better results than boys [33]. Therefore, the influence of gender on the performance on spatial orientation tasks in childhood is not clearly defined.

All the spatial orientation tasks are related to the other neuropsychological measures in preterm children, IQ and visuospatial abilities, and the magnitudes of these associations are larger than those found in controls. As expected, visuospatial abilities, especially those related to directionality and establishing spatial relations, are related to all the spatial orientation outcomes in the preterm group, but only to egocentric orientation in the at-term children. Regarding Route Finding administration, it can be assumed that 2D egocentric strategies are employed to solve the task because an allocentric strategy cannot be used efficiently due to the absence of landmarks. Therefore, preterm children would tend to also use allocentric strategies to deal with the Route Finding test and vice versa. Moreover, it seems that only preterm children also use mental rotation skills to orient themselves during spatial memory tests. Relationships between IQ and the other spatial tasks in preterm children are especially striking, although the functions involved are not the same, or even similar. These results reinforce the idea that preterm children use different functions to solve spatial orientation tasks. However, we also find that in controls, IQ is related to Egocentric part A. In general, fluid intelligence, included in the test, has been associated with working memory capacities [34]. Thus, it is logical that to perform this task, typically developing and preterm children would employ skills related to fluid intelligence. On successive spatial tasks, control children generalize strategies previously used to face these new tests, but this does not seem to be the case in preterm children.

Furthermore, we found that behavior is related to spatial orientation results, but curiously, these variables seem more relevant for controls than for preterm children. In both groups, we found that adaptive behaviors are related to better performance on spatial orientation. In the case of the controls, we also found that the variable Atypicality, related to the presence of psychotic symptoms, is related to worse Egocentric part B scores. There is not much literature that relates behavior to spatial orientation performance. However, behaviors such as withdrawal, attention problems, and aggressiveness have been found to affect spatial memory performance [31]. Thus, behavioral assessments seem to be relevant in completely understanding spatial orientation achievements during childhood.

With regard to spatial memory in real contexts, scores on the questionnaire completed by parents seem to be associated with experimental spatial orientation tasks, but only in control children. The items that assess short-term and working memory are associated with Egocentric Part A, which is more related to this function. In Part A, children are asked not only to remember the position of the cards, but also to inhibit previously memorized positions. On the other hand, the orientation items are associated with allocentric orientation. The lack of association between spatial orientation tests and the memory questionnaire in the preterm sample may indicate that spatial orientation tests are not a truly functional measure of spatial memory in preterm children. However, it should be taken into account that this questionnaire collects subjective information from parents and is not a direct measure of orientation.

In terms of perinatal risk factors, we found that factors related to IQ impairment were surgery and necrotizing enterocolitis; factors linked to visuospatial difficulties were caesarean delivery, CPAP, surgery, late onset sepsis, and intraventricular hemorrhage; and factors associated with the Egocentric test were surgery, necrotizing enterocolitis, and intraventricular hemorrhages; whereas Allocentric task performance was related to multiple delivery and intraventricular hemorrhages. Thus, visuospatial ability was most affected by different risk factors, followed by egocentric orientation, and, lastly, IQ and allocentric orientation. Furthermore, we found that undergoing early surgery was the risk factor related to the greatest number of cognitive dysfunctions, followed by intraventricular hemorrhage, late onset sepsis, necrotizing enterocolitis, and, lastly, CPAP and type of delivery (multiple/single and vaginal/caesarean). According to previous studies, early surgery in preterm children seems to be related to a greater risk of suffering future sensorineural disability [35], as well as cognitive impairment [36]. Specifically, our sample underwent surgery for hydrocephalus and necrotizing enterocolitis. It has been found that the risk of disability is higher in preterm children who have had an operation for ventricular drainage and bowel surgery [35], but the authors concluded that the type of surgery carried out is not as important as whether or not it took place. Early hemorrhages are related to a greater impact on neurodevelopment in very and extremely preterm children [37]. With regard to late onset sepsis, it has been related to memory, attention, and IQ impairment, but, contrary to our results, not to visuoperceptual abilities [38]. Lower IQ or developmental status is also found in preterm children with both necrotizing enterocolitis and sepsis [39]. Contrary to our results, previous studies show that the CPAP procedure does not seem to have an impact on neuropsychological outcomes in preterm children [40]. However, it should be kept in mind that when a newborn receives CPAP, it is often due to a previous respiratory complication that could have had an impact on the oxygen supply to the brain. Thus, for example, lower oxygen saturation in cerebral tissue is related to worse cognitive outcomes in preterm children [41]. Regarding multiple or single pregnancy, preterm twins seem to show lower language and visual processing outcomes than preterm single births [42]. Based on our results and scientific evidence, it appears that the factors related to greater neuropsychological dysfunction, mainly to visuospatial and spatial orientation skills, are surgical procedures, intra-periventricular hemorrhages, and multiple pregnancies. Surprisingly, and contrary to what was expected, neither gestational age nor birth weight was associated with neuropsychological performance. However, it should be taken into consideration that this study focused on children born preterm with a very low birth weight. Thus, the sample's relative homogeneity on these two variables may keep us from finding relationships.

Our study has some limitations. A more extensive neuropsychological evaluation protocol could allow us to analyze spatial orientation performance considering a greater number of influential factors. Likewise, inherent characteristics of the preterm sample lead to the same subject presenting several of the perinatal risk factors analyzed, and so we cannot determine which factors are causing the cognitive impairment.

Despite this, our study proposes including spatial orientation tasks in the neuropsychological evaluation protocols in order to detect possible deficits and design appropriate interventions. We have been able to verify that low birth weight preterm children from 5 to 7 years of age present difficulties in their allocentric spatial orientation capacities. In addition, their performance on spatial orientation seems to depend on visuospatial abilities.

Conflict of interest statement

None declared

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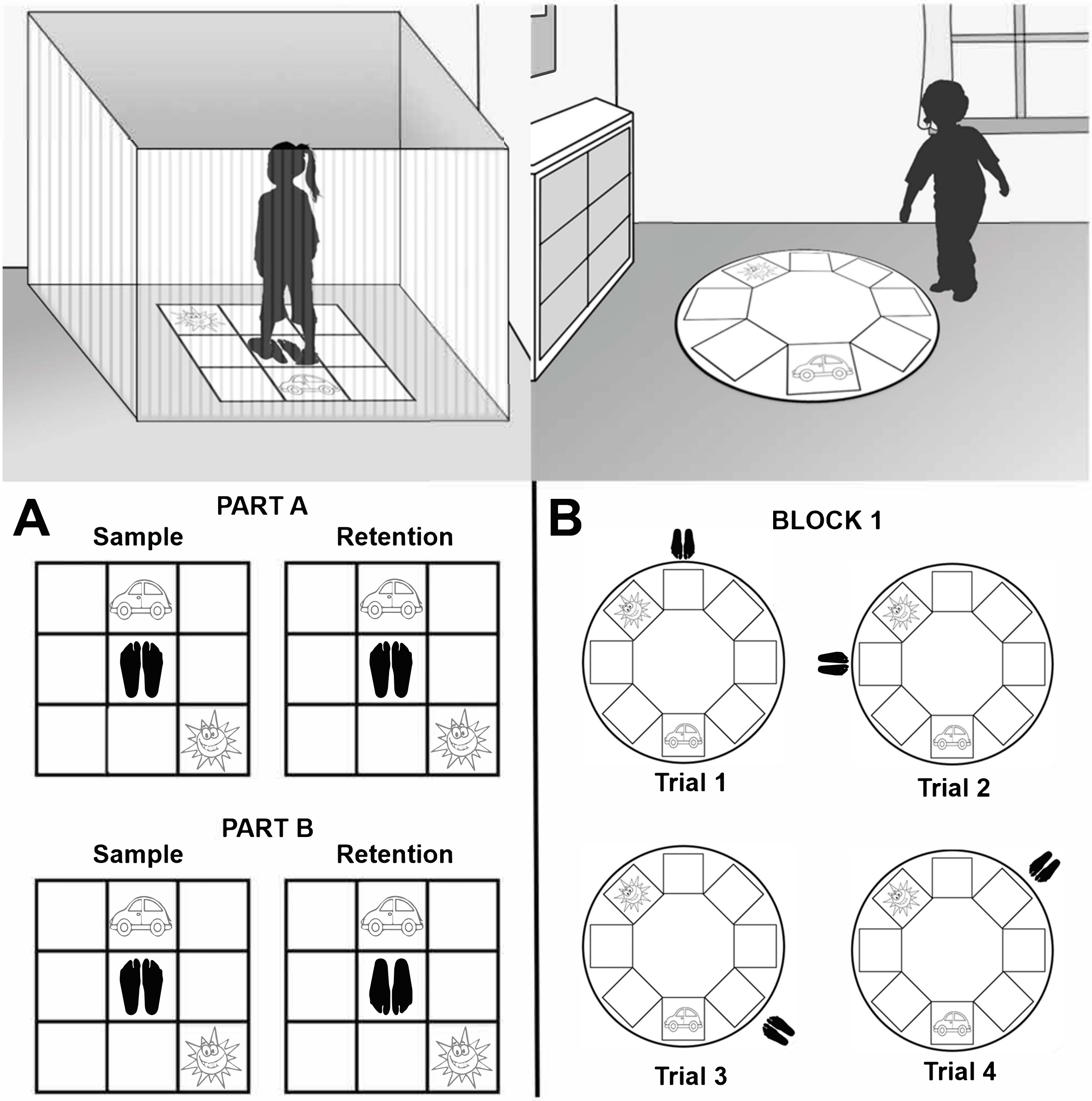
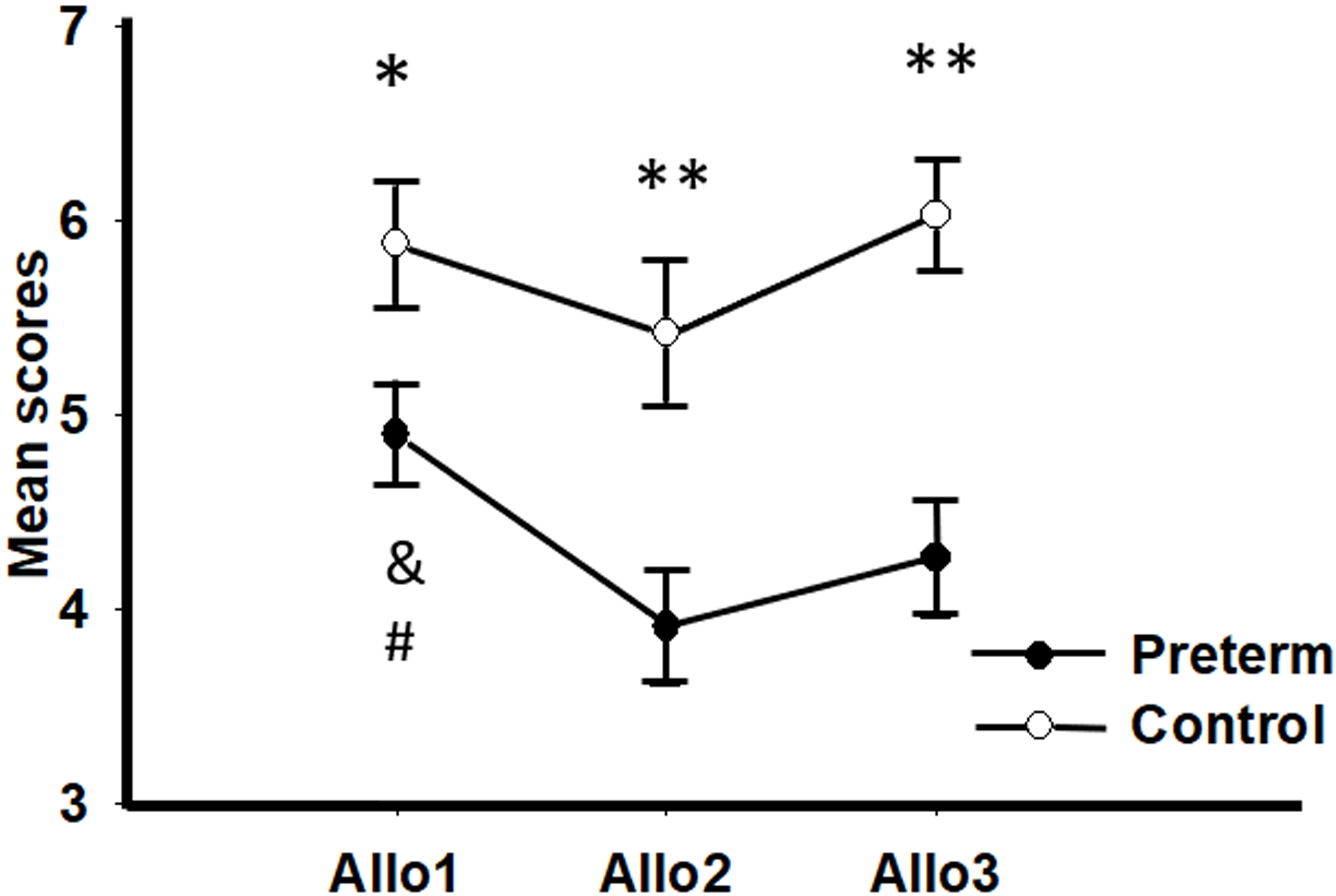
Figure Legends

Figure 1. Egocentric (A) and Allocentric (B) Spatial Memory Tests adapted to children. (A) Egocentric item example. In Part A, child is standing in the central square of the template in both sample and retention. In Part B, immediately after the examiner has removed the cards, the child is rotated (90º or 180º to the left or the right and then, he/she is asked to put each picture in the same places as before. (B) Allocentric Block example. While child's location varies in each trial, the position of the cards is always the same.

Figure 2. Comparison of allocentric blocks between preterm and control children (Mean and SEM). Control children show significantly better scores than premature in block 1 (Allo 1), block 2 (Allo 2) and block 3 (Allo 3) (* $p < 0.05$, ** $p < 0.01$). Preterm children perform significantly better in block 1 than in block 2 (& $p < 0.001$) and block 3 (# $p = 0.015$).



A
PART A
Sample
Retention
PART B
Sample
Retention
B
BLOCK 1
Trial 1
Trial 2
Trial 3
Trial 4



7
6
5
4
3
Mean scores
*
**
**
&
#
Preterm
Control
Allo1
Allo2
Allo3

Table 1. Distribution of the sample according to age, gender, and level of education of the mother in the preterm and control groups.

	Preterm			Control		
	N (%)					
Age	Boys (N)	Girls (N)	N (%)	Boys (N)	Girls (N)	N (%)
5 years	18	12	34.1	7	14	32.2
6 years	17	12	33	12	9	35.6
7 years	14	15	33	13	7	32.2
Maternal educational level						
Bachelor's degree	47.1%			82%		
Technical	29.9%			10%		
Secondary	14.9%			6%		
Primary	8%			2%		
Illiterate	0%			0%		

Table 2. Neonatal and neurodevelopmental description of the preterm sample (Mean and SD or %)

	Mean (SD)
Birth weight (grams)	1150.43 (240.01)
Gestational age (weeks)	30.12 (2.83)
APGAR test (1 minute)	6.97 (2.20)
APGAR test (5 minutes)	8.57 (1.50)
	N (%)
Intrauterine growth status	
Small for gestational age (<Pc10)	26 (29.54%)
Appropriate for gestational age	58 (65.90%)
Large for gestational age (>Pc10)	4 (4.54%)
Neurodevelopmental alterations	N (%)
Any developmental disorder	17 (19.5%)
ADHD	3 (3.4%)
Learning disorder	2 (1.1%)
Cerebral palsy	5 (5.7%)
Behavioral problems	3 (3.4%)
Autistic spectrum disorder	2 (2.3%)
Language disorder	10 (11.5%)

Table 3. Comparisons of preterm and control children on neuropsychological outcomes (Mean and SEM) on IQ assessed by the RIST, Geometric puzzles (GP), Route finding (RF), Egocentric Part A (EgoA), Egocentric Part B (EgoB), and Allocentric (Allo) tests. Statistically significant differences between groups are observed on the RIST, RF, EgoA and Allo (p<0.01).

	Preterm Mean (SEM)						Control Mean (SEM)						Significant Effects		
	Total Sample	Gender		Age			Total Sample	Gender		Age			Group	Gender	Age
		Boy	Girl	5	6	7		Boy	Girl	5	6	7			
RIST	90.51 (1.815)	90.65 (2.304)	90.33 (2.932)	89.87 (2.571)	92.86 (3.472)	88.83 (3.408)	109.56 (1.662)	112.28 (2.288)	106.40 (2.328)	108.62 (2.531)	109.19 (2.837)	110.55 (3.376)	**p<0.001**	p=0.267	p=0.875
GP	18.27 (0.616)	17.80 (0.743)	18.87 (1.035)	14.57 (0.657)	16.14 (0.684)	24.24 (0.843)	19.72 (0.510)	20.32 (0.713)	19.03 (0.723)	16.95 (0.505)	18.86 (0.508)	23.30 (0.921)	p=0.062	p=0.970	**p<0.001**
RF	2.94 (0.274)	2.94 (0.377)	2.97 (0.402)	1.57 (0.213)	2.86 (0.420)	4.48 (0.572)	4.38 (0.373)	5.19 (0.544)	3.53 (0.469)	3.05 (0.484)	4.05 (0.678)	6.05 (0.591)	**p=0.010**	p=0.164	**p<0.001**
EgoA	7.92 (0.238)	7.82 (0.338)	8.16 (0.328)	7.23 (0.392)	7.93 (0.480)	8.76 (0.316)	9.27 (0.131)	9.44 (0.162)	9.13 (0.208)	9.05 (0.263)	9.43 (0.202)	9.40 (0.210)	**p<0.001**	p=0.915	p=0.126
EgoB*	5.61 (0.252)	5.57 (0.317)	5.74 (0.411)	4.50 (0.324)	5.82 (0.466)	6.66 (0.428)	6.71 (0.273)	6.97 (0.411)	6.43 (0.358)	6.30 (0.471)	6.71 (0.489)	7.10 (0.464)	p=0.197	p=0.704	**p=0.047**
Allo total	12.97 (0.656)	12.45 (0.798)	13.92 (1.091)	9.77 (1.053)	14.71 (1.019)	14.97 (1.087)	17.37 (0.660)	18.52 (0.847)	16.17 (0.984)	15.05 (1.274)	18.05 (0.912)	18.95 (1.101)	**p<0.001**	p=0.901	**p=0.003**
Allo block 1	4.90 (0.253)	4.73 (0.330)	5.24 (0.395)	3.73 (0.377)	5.96 (0.343)	5.24 (0.485)	5.88 (0.321)	6.03 (0.451)	5.73 (0.465)	5.70 (0.529)	5.62 (0.567)	6.35 (0.586)	**p=0.014**	p=0.599	p=0.093
Allo block 2	3.91 (0.301)	3.67 (0.398)	4.29 (0.459)	2.93 (0.444)	3.79 (0.576)	5.14 (0.473)	5.42 (0.371)	6.10 (0.455)	4.63 (0.566)	4.05 (0.745)	6.14 (0.508)	5.90 (0.589)	**p<0.001**	p=0.707	**p=0.013**
Allo	4.16	4.04	4.39	3.10	4.96	4.59	6.03	6.32	5.80	5.30	6.29	6.60	**p=0.001**	p=0.805	**p=0.08**

block 3	(0.303)	(0.402)	(0.464)	(0.528)	(0.464)	(0.524)	(0.283)	(0.395)	(0.408)	(0.576)	(0.421)	(0.444)

* P values reported in Egocentric B are those obtained from the covariance analysis of Egocentric A

Table 4. Correlations of Egocentric (parts A and B) Spatial Memory Test and Allocentric (Total) Spatial Memory Test with neuropsychological outcomes from RIST, Geometric Puzzles, and Route Finding

		Preterm sample			Control sample		
		Egocentric A	Egocentric B	Allocentric total	Egocentric A	Egocentric B	Allocentric total
RIST	Pearson correlation	**.435****	**.230***	**.266***	**.278***	.238	.169
	P value	**.000**	**.032**	**.013**	**.033**	.069	.200
Geometric puzzles	Pearson correlation	**.470****	**.457****	**.409****	.087	.127	.244
	P value	**.000**	**.000**	**.000**	.514	.344	.065
Route finding	Pearson correlation	**.287****	**.397****	**.466****	**.274***	**.388****	.250
	P value	**.007**	**.000**	**.000**	**.038**	**.003**	.059

*p=0.05; **p=0.01