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Long-Term Influences of a Preterm Birth on Movement Organization and Side Specialization in Children at 4–8 Years of Age

ABSTRACT: This study explored upper-limb and head kinematics during unimanual goal-directed movements in children born preterm (PT) and full-term (FT) aged 4–8 years. Further, functional lateralization was investigated through side-specific kinematics and hand preference observations. Altogether, 141 children were included, divided into three sub-groups based on gestation week at birth (GW). Children born FT (38–41 GW) and moderately PT (33–35 GW) showed faster, smoother, and shorter movement trajectories than children born very PT (V-PT < 33 GW). Only children born FT expressed evident side differences that were characterized by smoother movements with the preferred side. Regarding hand preference, the children born V-PT showed increased rates of non-right-handedness compared with the other groups. Regardless of hand preference, the children born V-PT showed less well organized movements compared with the other groups. These findings suggest that spatio-temporal movement organization and side specialization at pre-/early school-age are affected by a PT birth, and more frequently so for children born before 33 GWs, indicating long-lasting influences on neuromotor development and specialization. © 2014 Wiley Periodicals, Inc. Dev Psychobiol

Keywords: preterm; handedness; laterality; child development; kinematics; motor performance

INTRODUCTION

Children born preterm (PT; <37 gestational weeks, GW) without known motor and/or neurological deviations have frequently been shown to exhibit higher rates of mild to moderate motor impairment compared with typically developing children born full-term (FT) (De Kieviet, Piek, Aarnoudse-Moens, & Oosterlaan, 2009; Edwards et al., 2011; Williams, Lee, & Anderson, 2010).

In a systematic review and meta-analysis by De Kieviet and colleagues (2009) a three- to fourfold increase in motor skill impairment was found in PT born populations without congenital anomalies compared with controls. Most studies investigating motor performance in children born PT have used standardized test batteries where manual dexterity and balance have been shown to be most severely affected (De Kieviet et al., 2009). To date, only a handful studies have investigated the organization and control of upper-limb movements in detail in infants and children born PT (Fallang, Saugstad, Grøgaard, & Hadders-Algra, 2003; Grönqvist, Strand Brodd, & von Hofsten, 2011; Sagnol, Debillon, & Debû, 2007; Toledo & Tudella, 2008). These studies have shown less optimal reaching (Fallang et al., 2003), less energy efficient movement paths (Grönqvist et al., 2011), and slower movements with increased

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adjustments in infants born PT at 4–8 months of age (Toledo & Tudella, 2008). Further, increased movement segmentation and movement duration have also been reported in children born very preterm (V-PT) at 3½ and 5 years of age (Sagnol et al., 2007).

The degree and rate of motor impairment have been shown to be higher in, but not confined to, children born extremely PT (≤ 27 GW) (Cooke, 2005; Foulder-Hughes & Cooke, 2003; Leversen et al., 2011) and with extremely low birth weights ($< 1,000$ g) (Foulder-Hughes & Cooke, 2003). Preterm birth is associated with an increased risk of neuromotor deviation related to early occurring excitotoxicity as sequelae to oxygen deprivation, hemorrhages, and/or infection/inflammation that may cause persistent and severe deviances in neurological development (Volpe, 2009). Excitotoxicity has detrimental effects on the functions of the central nervous system (CNS) with long-term effects on the development of the brain (De Kieviet, Zoetebier, Van Elburg, Vermeulen, & Oosterlaan, 2012; Volpe, 2009). Thus, a prominent risk associated with preterm birth is varying degrees of impaired sensory-motor functioning. The risk for severe sensory-motor impairment, as in cerebral palsy (CP), is most prevalent for the most immature infants, possibly as perinatal risk factors are more frequently occurring at earlier gestational ages (GAs).

It has further been shown that early occurring lesions and disruptions of the developing nervous system can cause alterations of the functional organization of the CNS (Lidzba, Wilke, Staudt, & Krägeloh-Mann, 2009; Staudt, 2007, 2010; Staudt et al., 2002). A directly observable manifestation of cerebral functional organization is handedness. The establishment of non-right hand (NRH) preference has been shown to be associated with low birth weight, preterm birth, and a higher level of neonatal risk factors (Marlow, Roberts, & Cooke, 1989; O'Callaghan, Burn, Mohay, Rogers, & Tudehope, 1993; Powls, Botting, Cooke, & Marlow, 1996). Further, a recent review and meta-analysis observed that children born preterm have more than a twofold likelihood of developing a NRH preference in comparison to children born FT (Domellöf, Johansson, & Rönnqvist, 2011). Most of the studies included in this meta-analysis investigated "handedness" as a secondary focus using hand preference questionnaires filled out by the child or parents or by observing the frequency of hand used during manual tasks. There is, however, a profound knowledge gap regarding how a preterm birth history might affect later side-specific movement performance and kinematics. One relevant approach to study this relation is by carefully investigating side-specific spatio-temporal characteristics of goal-directed arm-hand movements and associated head movements in children born PT. To

our knowledge, this is the first study to explore these relations in children born PT.

As a higher prevalence of NRH preference has been shown in populations born PT compared with those born FT (Domellöf et al., 2011), it is plausible that increased occurrence of left- and non-evident hand preferences are related to an altered organization of the brain caused by events associated with a preterm birth. It is also possible that the higher prevalence of NRH preference could be related to less efficient motor learning, which is in line with findings of deviations in synaptic plasticity mechanisms of the motor cortex in children born PT (Pitcher, Riley et al., 2012; Pitcher, Schneider et al., 2012). Consequently, increased and more specific knowledge of the association between brain functions and the organization of the motor system in the vulnerable population born PT could be of diagnostic relevance. As far as we know, only one previous study has employed movement registration technique (2-D digitizing tablet) to study motor performance with the respective hands in children born PT compared with children born FT (Sagnol et al., 2007). However, this study did not include a devoted research question regarding hand-use differences.

Thus, the main objectives of the present study were to explore differences between children born PT and FT with regard to the spatio-temporal organization of upper-limb movements, associated head movements and side specificity in relation to hand preference. The influence of different GAs within the group of children born PT on movement organization and the strength and classification of hand preference were further explored. Based on outcomes from previous studies, we hypothesized that the children born PT, V-PT in particular, would, in general, show less smooth and coordinated arm movement trajectories and display less evident side preference (preferred hand in specific manual tasks) compared with age-matched children born FT. Additionally, we expected that the children born PT would show more segmented head movement trajectories with longer 3D distances during task performance, especially when using their non- or less-preferred side as these movements might be less proficient and thus in need of more visual guidance.

METHODS

Participants

Sixty-eight children born PT (≤ 35 GW, range, 22–35, $M = 31.7$, $SD = 3.4$), 30 girls, aged between 4 and 8 years (M age at testing = 6.4, $SD = 1.7$) were recruited through records from the Norrland's University Hospital neonatal

intensive care unit, Umeå, Sweden. In addition, 80 age-matched (M age at testing = 6.4, SD = 1.8; 36 girls) children born FT; healthy at birth according to ICD-10, were recruited as a control group via birth records from the maternity ward at the same hospital. The included 4-year-old children born PT were tested at corrected age, that is, the 4-year-old children born FT were chronologically younger by the number of weeks the children born PT were premature. This was carried out to ensure that possible maturation effects related to the degree of prematurity were accounted for. The children born PT that were older than 4 years were deemed to have had sufficient time to catch up developmentally. Four of the participants born PT (1 girl aged 4.10 and 3 boys aged 4.3, 4.9, and 4.9) returned a few months later to perform the kinematic tests as they did not cooperate at the first occasion. In these cases, only data extracted from the second occasion were included in the analyses. A total of three children born PT (2 girls aged 4.2 and 4.5; 1 boy aged 4.0) were excluded from the data analyses due to CP diagnosis. Further, one boy (aged 4.9) was excluded from the kinematic analyses as he only performed the task with the preferred hand. A total of four children (2 girls aged 8.2 and 8.8; 2 boys aged 4.5 and 7.1) were excluded from the FT group due to cerebral pathology requiring surgery in infancy (n = 1), childhood epilepsy (n = 1), diagnosis of a genetic syndrome affecting cognitive and motor development (n = 1) and failure to perform the test battery due to excessive fussiness (n = 1). The final sample included in the analyses was 141 children; 65 born PT and 76 born FT. Medical background and demographics of the children born PT is presented in Tables 1 and 2 and the demographics of the children born FT in Table 2. There were no significant group differences in parental education (Table 2). All participants gave their consent and their parents signed an informed consent form for participation. The study was approved by the Umeå Regional Ethical Board and conducted in accordance with the Declaration of Helsinki.

Apparatus and Procedure

Lateral Preference. Hand preference was assessed through repeated observations of the children's interaction with different objects. The assessment was based on modified versions of the Edinburgh Handedness inventory (Oldfield, 1971) and Coren and Porac's (1980) laterality questionnaire. Handedness was assessed through observation of which hand the child used when drawing, cutting with scissors, hammering, opening of lids on a set of boxes, and throwing a ball. Each action was repeated at least three times. Objects were always presented at the child's midline. A handedness index was calculated by the equation $(R - L) / (R + L)$. This procedure results in an index ranging from -1 to 1 where negative values represent a leftward bias (left handed, LH) and positives a rightward bias (right handed, RH). Values ranging between $-.3$ and $.3$ were regarded as a non-evident hand preference (NEHP). For some of the analyses the children were split into groups according to their laterality index score where the children classified as having a

Table 1. Background Characteristics and Medical History in the Pre-Perinatal Period of the PT Children (N = 65)

	M (SD)	Range
Age at testing (years)	6.5 (1.7)	4–8.7
GA (weeks)	31.7 (3.6)	22.9–35.4
BW (g)	1708 (661)	404–2962
BW standardized	−1.04 (1.3)	−3.9–1.93
Birth length	41.1 (5.3)	27–49
Head circumference (cm)	29.5 (3.8)	20.4–35.5
Apgar 10	8.7 (.97)	5–10
Mothers education (years)	14.2 (2.7)	7–21.5
Fathers education (years)	13.4 (2.9)	5–21
	n yes (% yes)	
Female sex	29 (45)	
SGA	14 (22)	
Amnionitis	1 (2)	
Infection	29 (45)	
PPROM	10 (15)	
Preeclampsia/eclampsia	16 (25)	
RDS	21 (32)	
BPD	7 (11)	
Respirator	13 (20)	
PDA	12 (18)	
NEC	2 (3)	
ROP	16 (25)	
GR I–II	13 (20)	
GR III+	3 (5)	
Cerebral pathology in infancy	15 (23)	
IVH GR I–II	9 (14)	
IVH GR III+	3 (5)	
PVL	1 (2)	
Mild abnormality non classified	3 (5)	
Congenital malformations	10 (15)	
Mild	8 (12)	
Severe	2 (4)	

Note: cm, centimeters; SGA, small for gestational age; RF, risk factors; PPRM, preterm premature rupture of membranes; RDS, respiratory distress syndrome; BPD, bronchopulmonary dysplasia; PDA, patent ductus arteriosus; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity (all children with ROP had normal or corrected to normal visual acuity); GR, grade; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia.

NEHP were grouped with those having a LH preference. These two groups in combination were classified as children with a non-right hand (NRH) preference.

Movement Kinematics. The children were comfortably seated in front of a testing table where the height of the seat and its distance from the table was adjusted so all children could perform the task readily. Further, care was taken to ensure stable foot support. The children performed a goal-directed unimanual upper-limb task where small beads were picked, by use of pincer-grip, and threaded onto a thin metal

Table 2. Participant Demographics Presented by Group

	V-PT Children (<i>n</i> = 30)		M-PT Children (<i>n</i> = 35)		FT Children (<i>n</i> = 76)	
	<i>M</i> (SD)	Range	<i>M</i> (SD)	Range	<i>M</i> (SD)	Range
Age (years)	6.9 (1.7)	4–8.7	6.9 (1.6)	4–8.7	6.4 (1.8)	3.7–8.5
GA (weeks)	28.7 (2.8)	22.9–32.7	34.2 (.52)	33.3–35.4	40.3 (1.0)	38–41.9
BW (g)	1,173 (438)	404–2,106	2,167 (436)	1,367–2,962	3,696 (408)	2,910–4,790
Mothers education (years)	13.5 (2.8)	7–21.5	14.9 (2.4)	8–19	14.6 (2.6)	9–25
Fathers education (years)	13.3 (2.4)	9–17.5	13.4 (3.3)	5–21	14.0 (3.1)	9–20
Girls (<i>n</i> %)	11 (37)		18 (51)		34 (45)	

Note: FT, born full-term; PT, born preterm; M-PT, born moderately PT; V-PT, born very PT.

rod sequentially. The task required midline crossings and the distance between the beads and the rod was 36 cm. This task has been developed for use with optical recordings and is challenging and engaging for children (see Domellöf, Fagard, Jacquet, & Rönnqvist, 2011; Johansson, 2012). It is a task with high demand on coordination and control of upper-body movements that includes visuomotor integration, motor planning, fine digit control, and gross motor function. Thus, fast movements with high precision can be considered as a result of successful movement planning and sensorimotor integration that results in a dynamic movement with few corrections.

The goal-directed upper-limb movements were recorded by use of a six-camera optoelectronic system (ProReflex, Qualisys Inc., Gothenburg, Sweden). A total of nine spherical passive markers were affixed with skin friendly adhesive tape to the left and right shoulders (diameter = 29 mm), elbows (19 mm), wrists (12 mm), and index fingers (7 mm). A marker (12 mm) was also affixed to the participants' forehead. The markers affixed to the index fingers were not accepted by some of the younger children (13 in total) thus, not included in the statistical analyses (see Fig. 1(A) for marker placement, experimental task, and (B) associated 3D movement trajectories during performance). The rod was equipped with a centralized half-spherical marker at its base (7 mm). The children were informed to pick and thread as many beads as possible, taking only one bead at the time, during a pre-set recording time of 30 s. The sampling frequency was 120 Hz. All children familiarized themselves with the task by picking and threading three to four beads, one at the time, with each hand. The experimental session consisted of a total of six trials, three with each hand in a counterbalanced order with the starting hand being randomized across children. Simultaneous video recordings, time synchronized with the onset/offset of the optoelectronic measurement system, were made to enable clarifications during data processing. The number of successful pick-to thread-to pick (PTP) cycles was extracted and unsuccessful trials were discarded in this process.

The criteria used for defining the onset and offset of the PTP cycle were the frame where the tangential velocity of the wrist marker was 60 mm/s and decreasing. The video recordings were used to verify the correct use of these criteria. The included children born PT completed 2,960 (*M* = 46) success-

ful PTP cycles and a total of 146 (4.9%) cycles were discarded due to dropping the bead or taking two or more beads at a time. The included control children completed 4,148 (*M* = 55) successful PTP cycles and a total of 203 (4.9%) cycles were discarded due to pick or drop errors. For inclusion in the analyses of the kinematic outcomes, the children had to perform at least two successful PTP cycles with both hands. If the children did not show an evident hand preference based on the outcomes from the laterality observations, the hand used most frequently for drawing or writing was used in the classification of preferred or non-preferred side for the analyses based on the kinematic data.

Methods for Analyses

Kinematic Data Analyses. Small marker occlusions (≤ 10 frames) were pre-set to be gap filled by the system software. Before accepting such gap fills, they were visually inspected and altered in cases where the fill was deemed incorrect. All recordings with larger gaps (maximum of 20 frames, *n* = 7) were manually filled if it could be reliably done. The suitability/reliability of all larger gap fills was checked in Z-, Y-, and X-plane, acceleration profile and velocity profile before accepting them. Prior to analyses, all 3D data (exemplified in Figs. 1A and 2B) were smoothed using a second order 12 Hz Butterworth filter. By use of customized MATLAB (The Mathworks Inc., Boston, MA) scripts, the cumulative (3D) distance (accumulated movement distance) and the number of movement units (MUs, segmentation of movement trajectories; exemplified in Fig. 2C) were extracted for the markers attached to the head and wrists. A MU is defined as an acceleration phase followed by a deceleration phase with an accumulated increase or decrease in velocity of at least 20 mm/s and an acceleration or deceleration exceeding 5 mm/s² (von Hofsten, 1991). Further, the duration of each PTP cycle was extracted (see Fig. 2 (A) for examples of displacement in the horizontal plane, (B) a velocity profile with MUs, and Fig. 1B for 3D movement trajectories during performance).

Statistical Analyses. To analyze the possible effect of GA, the children born PT were divided into two sub-groups based

FIGURE 1 (A) Photograph of a FT girl (8 years of age) depicting marker placement and the set-up of the goal-directed upper-limb task. *Photograph printed with permission.* (B) Example of a 3D spatial plot including head, left (L) shoulder, elbow and wrist movement trajectories during the 30 s pick-to thread-to pick task (of an 8-year-old girl) and with the bar position marked.

on their GAs: moderately preterm (M-PT) = GW 33–35, $n = 35$, and very preterm (V-PT) = GW < 32 + 6, $n = 30$ (see Table 2 for group specifics). Pearson's correlations were used to explore the consistency among the shoulder, elbow and wrist and the influence of age at testing on movement kinematics. In these analyses, data on both axes were continuous (no bivariate distribution) and conversion to z-score was thus not needed. As data were not normally distributed, Kruskal–Wallis test was applied to test differences in the laterality index between the groups. Focused comparisons were made to follow up significant effects using Mann–Whitney U tests with Bonferroni corrected p -values ($.05/3 = .017$). A version of Cohen's d based on the Z-values ($r = z/\sqrt{N}$) was used as effect size estimate (Rosnow & Rosenthal, 1996). Inspections of normality revealed that the kinematic data could be regarded as principally normally distributed, further confirmed by analyses with log 10 data. Thus, the kinematic outcomes were analyzed by MANOVAs with side (preferred/non-preferred) and group (FT, M-PT, V-PT) as categorical predictors. Based on the correlational analyses of the kinematics of the shoulder, elbow, and wrist these outcomes were mean valued for each side to create a composite score across the arm that was used in the main analyses. To further verify the composite score across the arm, the shoulder, elbow, and wrist markers were analyzed by separate analysis of variance (ANOVAs) to determine group effects. Side differences were further analyzed within each group by dependent samples t -tests. Due to technical measurement errors and marker refusals, the head marker was missing for one child in the non-preferred condition in the group born V-PT and four children for both sides in the group born FT. Further, data for the arm were missing for the non-preferred side for four children and for the preferred side for three children born V-PT. Thus, the number of children differs

slightly in the analyses. To investigate possible age effects on the kinematic outcomes and laterality index score MANCOVAs and Spearman's correlations were conducted. Age trends were found in all kinematic parameters but using age as a continuous covariate in the statistical analyses only contributed marginally to the effect sizes and p -values and did not have any effect on the main effects for group, thus, it was omitted from the analyses. Significant effects from the variance analyses were followed up by Unequal numbers honestly significant difference test and partial eta square (η^2_p) was used as the effect size measure. Bonferroni correction was not applied to the kinematic data due to the risk for excessive power reduction involved in this procedure when the outcome variables are related (Bland & Altman, 1995). Significant results are reported on the alpha level of <.05, <.01, <.001, and <.0001. Only test statistics for significant findings are reported throughout.

RESULTS

Laterality Index

There was a significant difference between the groups on the index values derived from the frequency based assessment, ($H(2) = 9.61$, $p < .01$; mean ranks: FT = 77.62; M-PT = 73.71; V-PT = 51.07). The follow-up analyses showed that the group born V-PT had significantly lower ranked index values compared with the group born FT ($U = 710$, $p < .01$, $d = .29$). No significant difference was shown between children born M-PT and V-PT ($p = .25$) nor between the children born FT and M-PT ($p = .63$). When excluding children

FIGURE 2 (A) Illustrations of horizontal (x) displacement of the head and the left (L) shoulder, elbow, and wrist of a FT born child (4.5 years old boy) where 8 pick-to thread-to pick cycles were performed, (B) velocity profile of the same displacement as shown in figure (A), and (C) velocity profile of the wrist displacement plotted over 4 s of the same trial as in figure (A) and (B) with the MUs identified as sub-units of the pick-to thread-to pick task performed.

Note: The circles on the respective velocity trajectory mark the onset/offset of each MU, where + indicate the peak-maxima and the local-minima within respective MU.

Table 3. Mean Values and Standard Deviations of Laterality Index and Related Handedness Classification Presented by Group and Overall for the PT Group

Group	Lat Index-Hand	RH	NEHP	LH	NRH
	<i>M</i> (<i>SD</i>)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
FT (<i>n</i> = 76)	.77 (0.35)	71 (93)	3 (4)	2 (3)	5 (7)
M-PT (<i>n</i> = 35)	.73 (0.42)	32 (91)	1 (3)	2 (6)	3 (9)
V-PT (<i>n</i> = 30)	.52 (0.54)	23 (77)	3 (10)	4 (13)	7 (23)
Overall PT (<i>n</i> = 65)	.63 (0.49)	55 (85)	4 (6)	6 (9)	10 (15)

Note: Lat, laterality; FT, born full-term; PT, born preterm; M-PT, born moderately PT; V-PT, born very PT; RH, right hand preference (lat index value $>.3$), NEHP, non-evident hand preference (lat index value $-.3$ to $.3$); LH, left hand preference (lat index value $<-.3$); NRH, non-right hand preference (lat index value $.3$ to -1).

classified as having a NRH preference (laterality index scores between $.3$ and -1), the group difference was close to significance ($p = .07$) where the children born V-PT still had the lowest mean rank score (V-PT = 47.89; M-PT = 64.02; FT = 67.50). When considering the frequency (%) of children classified as having a NRH preference, the children born PT showed increased rates compared with the children born FT, especially prominent in the group of children born V-PT. Age at testing did not correlate significantly with the laterality index score within any of the groups. Mean values and standard deviations of the laterality index and the categorical frequency distribution of handedness within the groups are shown in Table 3.

Associations Between Age at Testing and Kinematic Outcome Within the Groups

Significant correlations between age and movement performance were shown within all groups (see Fig. 3A–J for correlations between age at testing and kinematic outcomes by side within the groups). Independent of side, these relations were characterized by decreased movement duration, movement segmentation and 3D distance with increasing age. These results are also in line with the covariance outcomes from the MANCOVAs where age at testing was significant in most analyses.

Associations Between the Number of MUs and 3D Distance of the Shoulder, Elbow, and Wrist Within the Groups

Significant correlations were shown between both the mean number of MUs and the mean 3D distance across the arm (shoulder, elbow, wrist composite) within all the groups (see Table 4). These correlations were high for both the preferred and non-preferred side. In general, the correlations were higher for the number of MUs than the 3D distance and higher between the wrist

and elbow than between the shoulder and wrist, and the elbow and shoulder. The children born V-PT had the highest Pearson's r -values across the arm.

Duration

A significant main effect for group was shown ($F(2, 275) = 17.42$, $p < .0001$, $\eta^2_p = .11$) where the children born V-PT displayed longer movement durations of the PTP cycles than both the children born FT ($p < .0001$) and M-PT ($p < .0001$). Mean values and standard deviations by group and side are presented in Table 5. When the analysis was conducted including only the children classified as right-handed, the main effect for group remained ($F(2, 243) = 8.52$, $p < .001$, $\eta^2_p = .07$) where the children born V-PT generally had longer durations than the children born M-PT ($p < .01$) and FT ($p < .01$). Hence, the children born V-PT had significantly longer movement durations than the children born M-PT and FT regardless of hand preference (see Fig. 4A). No significant effects for side or group by side interactions were shown in either analysis.

Movement Segmentation (MUs)

Group was a significant categorical predictor for the mean number of MUs across the arm ($F(2, 269) = 8.81$, $p < .001$, $\eta^2_p = .06$; see Table 5). The children born V-PT showed more segmentations of the movement trajectories across the arms than both the children born FT and M-PT ($p < .001$ and $p < .001$, respectively). Regarding MUs of the head, group was again significant ($F(2, 267) = 8.76$, $p < .001$, $\eta^2_p = .06$) with the children born V-PT showing significantly more segmentations than the children born FT and M-PT ($p < .001$ and $p < .001$, respectively). When individuals classified with a NRH preference were excluded, group was still significant ($F(2, 240) = 3.28$, $p < .05$, $\eta^2_p = .03$) where the children born V-PT had increased segmentations across the arm (see Fig. 4B). Further, the number of segmentations of

FIGURE 3 Correlations, regression line shown, between age at testing and mean (M) wrist movement duration, M 3D head and across arm movement distance, and M number of head and across arm movement units (MUs) during performance with the preferred (A–E) and non-preferred (F–J) side for the full-term (FT), moderately preterm (M-PT), and very preterm (V-PT) born children. The r -value (Pearson's correlation coefficient) and its significance level are shown by group within each graph (* $p < .05$; ** $p < .01$; *** $p < .001$). The x-axis denotes age at testing in all graphs.

Table 4. Correlations Between Kinematic Outcomes of the Shoulder, Elbow, and Wrist Presented by Side Within the Groups

MUs Preferred Side				MUs Non-Preferred Side			
M-PT	Shoulder	Elbow	Wrist	M-PT	Shoulder	Elbow	Wrist
Shoulder	—	.87*	.91*	Shoulder	—	.80*	.77*
Elbow	.87***	—	.98*	Elbow	.80***	—	.94*
V-PT	Shoulder	Elbow	Wrist	V-PT	Shoulder	Elbow	Wrist
Shoulder	—	.96*	.95*	Shoulder	—	.94*	.95*
Elbow	.96***	—	.98*	Elbow	.94***	—	.98*
FT	Shoulder	Elbow	Wrist	FT	Shoulder	Elbow	Wrist
Shoulder	—	.84*	.86*	Shoulder	—	.87*	.86*
Elbow	.84**	—	.97*	Elbow	.88**	—	.96*
3D Distance Preferred Side				3D Distance Non-Preferred Side			
M-PT	Shoulder	Elbow	Wrist	M-PT	Shoulder	Elbow	Wrist
Shoulder	—	.75*	.64*	Shoulder	—	.66*	.66*
Elbow	.75***	—	.93*	Elbow	.66***	—	.94*
V-PT	Shoulder	Elbow	Wrist	V-PT	Shoulder	Elbow	Wrist
Shoulder	—	.82*	.85***	Shoulder	—	.82*	.86*
Elbow	.82***	—	.96***	Elbow	.82***	—	.95*
FT	Shoulder	Elbow	Wrist	FT	Shoulder	Elbow	Wrist
Shoulder	—	.69*	.60*	Shoulder	—	.71*	.65*
Elbow	.70***	—	.92*	Elbow	.71***	—	.96*

* $p < .01$; ** $p < .001$; *** $p < .0001$.

Note: FT, born full-term; PT, born preterm; M-PT, born moderately PT; V-PT, born very PT.

the head was still significantly differing between the groups ($F(2, 238) = 4.60$, $p < .01$, $\eta^2_p = .04$) where the children born V-PT had significantly more MUs compared with the children born FT ($p < .05$) (see Fig. 4B). No side effects or interactions were shown in any of the analyses.

3D Distance

The mean 3D distance across the arm differed between the groups ($F(2, 269) = 5.35$, $p < .01$, $\eta^2_p = .04$; Table 5) where the children born V-PT had longer movement paths than did the children born FT ($p < .01$). In terms of the 3D distance of the head, the groups differed significantly ($F(2, 267) = 9.80$, $p < .0001$, $\eta^2_p = .07$; Table 5) with the children born V-PT displaying longer movement paths than the children born FT ($p < .001$) and M-PT ($p < .0001$). No significant side or interaction effects were shown in any of the analyses. Further, no significant effect for side or interaction between side and group was shown when the children classified with a NRH preference were excluded from the analysis. This suggests that the children born V-PT with a NRH preference were driving the group effect shown in the analysis including all children (see Fig. 4C).

DISCUSSION

In this study, we explored movement organization, side-specific movement performance and hand preference in children born very preterm (V-PT; <33 GWs) and moderately preterm (M-PT; 33–35 GWs) compared with children born full-term (FT), all at 4–8 years of age. Although most of the children born PT were classified as right-handed, the group of children born V-PT had significantly lower laterality index scores compared with both the groups of children born FT and M-PT. Interestingly, only the group of children born FT showed significant within-group side differences in terms of kinematics where performance with the preferred side was smoother than the non-preferred side (Table 5). Furthermore, regardless of side, the group born V-PT had in general significantly increased movement duration, segmentation and 3D distance across and within the arm compared with the group of children born FT and M-PT. In addition, more head movements were shown compared with their FT and M-PT born peers. Most of these differences remained when only children classified as right-handed were included, indicating that a V-PT birth in general affects both movement performance and hand dominance, although, the right-handed

Table 5. Kinematic Outcomes Presented by Side and Group

	Group					
	FT		M-PT		V-PT	
	Pref <i>M</i> (SD)	N-pref <i>M</i> (SD)	Pref <i>M</i> (SD)	N-pref <i>M</i> (SD)	Pref <i>M</i> (SD)	N-pref <i>M</i> (SD)
MUs (n)						
Shoulder	22.6 (9.3)	26.5 (9.4) ^{aaa}	23.9 (11.3)	24.5 (8.6)	29.1 (15.7)	30.0 (14.9) ^b
Elbow	13.8 (5.5)	15.0 (5.9) ^a	13.4 (5.7)	13.4 (4.7)	18.6 (9.9)	18.0 (9.7) ^b
Wrist	10.6 (4.0)	12.0 (4.8) ^{aa}	11.0 (4.7)	11.1 (3.4)	16.6 (10.1)	15.4 (8.2) ^b
Across arm	15.7 (6.0)	17.8 (6.4)	16.1 (7.0)	16.5 (5.2)	21.4 (11.1)	21.2 (10.5)
Head	14.0 (7.7)	16.9 (7.5)	14.6 (8.0)	15.9 (6.5)	20.3 (13.2)	20.8 (9.0)
3D distance (mm)						
Shoulder	141 (54)	148 (55)	131 (42)	137 (47)	165 (80)	164 (86) ^c
Elbow	622 (123)	640 (151)	598 (92)	595 (89)	667 (139)	672 (150) ^c
Wrist	837 (152)	856 (158)	826 (89)	819 (89)	934 (174)	8926 (168) ^b
Across arm	533 (102)	548 (116)	518 (70)	522 (68)	581 (123)	582 (125)
Head	269 (90)	281 (106)	252 (80)	266 (86)	339 (148)	345 (186)
Duration (s)	2.9 (.8)	3.1 (.8)	2.9 (.9)	3.0 (.7)	3.8 (1.5)	3.9 (1.5)

Note: FT, born full-term; PT, born preterm; M-PT, born moderately PT; V-PT, born very PT; *n*, number; mm, millimeter; *s*, seconds; Pref, preferred side; N-pref, non-preferred side.

^aSignificant within group side difference as determined by dependent samples *t*-test (^a*p* < .05; ^{aa}*p* < .01; ^{aaa}*p* < .001).

^bV-PT born group significantly differs from the M-PT and FT born group (^b*p* < .05).

^cV-PT born group significantly differs from M-PT born group (^c*p* < .05) as determined by ANOVAs.

children born V-PT were also less lateralized than the children born M-PT and FT. Based on these findings, we suggest that studies focusing on side differences and related developmental trajectories in preterm born populations would benefit from applying detailed methods for investigations of sensory-motor functions to enable detection of even subtle differences in movement organization and control.

Side Preference and Movement Performance

The finding of a weaker lateralization and increased rate of NRH preference in the group of children born V-PT is in line with previous studies showing similar distributions (e.g., Ashton, 1982; Harding, Walker, Lloyd, & Duffty, 2001; Luciana, Lindeke, Georgieff, Mills, & Nelson, 1999; O'Callaghan et al., 1993; Ross, Lipper, & Auld, 1992). The over-representation of a NRH preference in children born PT has been theorized to be caused by early occurring disruption in brain development (Bakan, 1977; Bishop, 1990; Satz, 1972; Soper & Satz, 1984), occurrence of birth stressors (Coren, 1995), and/or preterm birth in its own right (Marlow, Hennessy, Bracewell, & Wolke, 2007; O'Callaghan et al., 1993; Powls et al., 1996; Ross, Lipper, & Auld, 1987; Sagnol et al., 2007; Saigal, Rosenbaum, Szatmari, & Hoult, 1992). More recently evidence has emerged which implicates deficits in mechanisms of neuronal plasticity (Pitcher, Riley et al., 2012; Pitcher,

Schneider et al., 2012) and lack of interhemispheric motor inhibition reflecting a developmental delay or deviation in the development of hemispheric dominance in children born PT (Flamand, Nadeau, & Schneider, 2012). These findings may both be related to impairment in the establishment of a specialized hand. Further, Flamand and colleagues (2012) noted that these deviances in hemispheric dominance were larger in the children born most prematurely which is in accordance with the increased rates of a NRH preference and lack of side-specific motor performance within the group of children born V-PT in the present study. Although differences were shown between the group of children born V-PT and the groups born M-PT and FT on the frequency-based handedness assessment, significant side differences were not found with regard to the kinematic outcomes across the arm and head. However, compared with the groups of children born PT, the group of children born FT consistently showed more evident side differences, especially on outcomes related to movement segmentation of the arm and duration where performance with the preferred hand was smoother and faster compared with the non-preferred hand. Further, when investigating within-group side differences only the children born FT showed significantly smoother performance of the shoulder, elbow and wrist of the preferred side. Interestingly, the M-PT children did not differ from the FT children on any of the kinematic parameters,

FIGURE 4 Box-plots showing mean movement duration (A), mean number of MUs (B), and mean 3D distance by pick-to thread-to pick cycle. Plots are shown by group and further sub-categorized according to right-hand preference (RH) and non-right-hand preference (NRH), the x-axis denotes hand preference in all graphs. In all plots the mean is denoted by the □, the box shows the standard error and the whiskers indicate 95% confidence interval.

Note: s, seconds; n, number; mm, millimeter; FT, full-term; M-PT, moderately preterm; V-PT, very preterm; RH, children categorized as right-handed; NRH, children categorized as non-right-handed.

although, no significant side differences were shown within the M-PT group suggesting an equally good performance with both sides.

The group of children born FT showed increased segmentation of the head while performing the task with their non-preferred hand. Similar results, although non-significant, were shown in the group of children born M-PT. This finding could be interpreted as compensatory head movements when performing with the non-preferred hand due to an increased need of visual input to guide performance compared to when using the preferred hand. Contradictory to our hypothesis, the children born V-PT did not show increased head movements during performance with the non-preferred hand which may be related to the general lack of side differences in performance within this group of children (i.e., performance with both the preferred and non-preferred side needs visual input to the same extent). Another possible explanation is that the increased movement variability of the head during performance of the bead-threading task seen in children born FT is related to more developed movement dynamics manifested in an increase in degrees of freedom in their upper-body movements (including the head, trunk, arm, and hand) compared with children born V-PT. Thus, more degrees of freedom increase the likelihood of different performance profiles with the preferred and non-preferred side as observed in the group of children born FT. A further possibility is that the lack of side differences in head movements in the group of children born V-PT could reflect greater postural instability, although not measured here, as seen in children with fetal alcohol syndrome (FAS) (Domellöf, Fagard *et al.*, 2011).

When the kinematic data were analyzed including only the children classified as right-handed, the children born V-PT still displayed significantly longer durations and increased number of segmentations although there was a substantial lowering of mean values (see Fig. 4A–C). These findings suggest a general effect of a V-PT birth on movement performance that may not be associated to hand preference *per se*. However, the children classified as right-handed in the group born V-PT also showed a trend towards reduced laterality scores compared with the right-handed children of the other groups. This has also been shown in children with FAS (Domellöf, Rönnqvist, Titran, Esseily, & Fagard, 2009). Thus, it is possible that the general decrease of side specialization found in the children born V-PT is related to poorer movement organization in general. Our findings suggest that a bias towards a specific side in terms of more advanced upper-limb movement control is manifested in children born FT, whereas less evident expressions of functional asymmetries are persistent in

primarily the group of children born V-PT. We suggest that detailed assessments of the causal relations and associations between risk factors in the pre- and perinatal period, brain structure and function, lateral preference, motor learning, and side-specific motor performance must be carried out to better understand the underlying mechanisms of the observed findings.

Effects of Age at Testing on Side Preference and Movement Performance

Age at testing did not influence the lateral preference as assessed by the laterality observations suggesting that hand preference at the ages of 4–8 is stable, regardless of maturity level at birth. Studies have shown that most children have a fluctuating hand preference during infancy (Corbetta & Thelen, 1999; Rönnqvist & Domellöf, 2006) although others have shown it to be stable, with increasing preference, during 6–14 months of age (Ferre, Babik, & Michel, 2010; Hinojosa, Sheu, & Michel, 2003; Michel, Tyler, Ferre, & Sheu, 2006). Other suggest that it is around the age of 3 that hand preference stabilizes (Corbetta & Thelen, 1999; Rönnqvist & Domellöf, 2006). In accordance, the increased frequency of NRH shown in the group born V-PT does not appear to be under developmental change at these ages. As expected, large age effects were apparent on all kinematic outcomes suggesting that age related processes are influencing the kinematic performance in all GA groups (see Fig. 3A–J). In general, with increasing age, the duration and 3D distance became shorter and the segmentations fewer of both the preferred and non-preferred side. Thus, movements on both sides appear to become increasingly efficient with age, a finding that may be explained by both maturational effects and increased experience. These results are consistent with findings showing a gradual increase in smoothness of movement trajectories and a gradual decrease in duration of goal-directed upper-limb movements between 4 and 12 years of age (Kuhtz-Buschbeck, Stolze, Jöhnk, Boczek-Funcke, & Illert, 1998). Interestingly, when investigating the age effects by side within each of the groups, it became apparent that the largest GA group differences were shown for the youngest children and the performance of the 7- to 8-year-old were shown to be fairly equal between the GA groups (see Fig. 3A–J). As the present study does not have a developmental design, longitudinal studies are needed to explore developmental effects with regard to both biological maturation and experience-related changes on movement kinematics within populations of children born PT. Such studies would help to establish if and when children born PT have had sufficient time to catch up in terms of movement performance.

Across Arm Correlations

The correlations between the shoulder, elbow, and wrist (across the arm) within the group born V-PT may suggest a tighter proximo-distal joint coupling. It is possible that tighter joint couplings are a strategy used to reduce the number of degrees of freedom resulting in more proximal control of movements which increases end-point accuracy. Such strategy has been shown in children with hemiplegic cerebral palsy (Domellöf, Rösblad, & Rönqvist, 2009; Rönqvist & Rösblad, 2007) and in children with FAS (Domellöf, Fagard et al., 2011). However, appropriate time-series analyses of intra-joint couplings must be carried out to verify if such a relationship exists in children born PT.

Kinematic Effects Related to GA

In general, the children born V-PT were slower in their execution of the task and showed increased segmentation and distance of their movement trajectories than did the children born M-PT and the FT. This finding is in line with the differences found by Sagnol et al. (2007) where children born V-PT at 2–6 years were shown to have slower and more segmented movements during a visuo-manual aiming task compared with a FT control group. Further, several other studies using gross and fine motor test batteries have shown higher rates of a general deficit in sensory-motor functioning in children born V-PT (e.g., de Kieviet et al., 2009; Edwards et al., 2011). In a meta-analysis by Williams and colleagues (2010) where motor skill was investigated in children born <37 GW, the motor impairments could not be statistically analyzed by GA or BW but the data did implicate higher prevalence of motor impairments in the studies involving children born with the lowest GAs and BWs. The present findings suggest that such less favorable outcome in tests of motor skill may be manifested in poorer sensory-motor coordination and control as revealed by kinematic analysis. Further, the poorer sensory-motor coordination and control are of increasing magnitude in lower GAs and BWs. Future kinematic studies should also include general tests of motor skill to describe the association between the detailed outcomes from kinematic registrations and more general motor test battery outcomes.

CONCLUSION

This study found that children born V-PT, without previously identified sensory-motor deviations, showed increased rates of NRH preference, weaker hand preference scores and less optimal movement control compared with their peers born FT and M-PT. The less

optimal movement control shown in children born V-PT was not explained by the children classified as having a NRH preference, although the movement performance may be influenced by an apparent less evident right-hand preference among the children born V-PT classified as right-handed. Further, side differences in movement performance were only shown within the group of children born FT. The most sensitive kinematic outcome was shown to be spatio-temporal segmentation. Thus, this study demonstrates the importance of investigating performance measures associated with movement execution when studying side differences and handedness. To verify the present results, longitudinal studies utilizing a kinematic approach when exploring both hand preference and side-specific movement performance are crucial. Such studies would enable an evaluation of the stability of side differences as well as the developmental trajectory of motor performance in general in children born at different GAs.

NOTES

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