Periventricular leucomalacia and preterm birth have different detrimental effects on postural adjustments

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Summary
Postural adjustments during sitting on a moveable platform were assessed by means of multiple surface EMGs of neck, trunk and leg muscles and kinematics in three groups of children, aged 1½–4½ years. The first group consisted of 13 preterm children (born at a gestational age of 25–34 weeks), whose neonatal ultrasounds had shown distinct lesions of the periventricular white matter (PWM). The second group was the preterm control group, consisting of 13 preterm children with normal neonatal brain scans, matched to the PWM group with respect to gestational age at birth, birth weight, sex and age of postural assessment. The third group was formed by 13 healthy children born at term and matched to the PWM group with respect to sex and age at examination. In addition to the postural assessment an age-specific neurological examination was carried out. Three of the children of the PWM group developed a cerebral palsy syndrome, nine showed minor neurological dysfunction and one child was neurologically normal. In the preterm control group one child showed minor neurological dysfunction, while the remaining 12 children of this group and all children of the full-term group were neurologically normal. The postural assessment revealed that preterm birth was associated with two types of postural dysfunction. One dysfunction was related to the presence of a PWM lesion and consisted of a limited repertoire of response variation. The other dysfunction was not related to the presence of a PWM lesion, but to preterm birth itself. It consisted of a change in the ability to modulate the postural responses. Preterm children showed a higher sensitivity to platform velocity than full-term children, and they lacked the capacity to modulate EMG amplitude with respect to initial sitting position.

Keywords: prematurity; periventricular leukomalacia; postural control; EMG; neurological development

Abbreviations: HAM = hamstring muscles; NE = neck extensor muscles; NF = neck flexor muscles; PWM = periventricular white matter; RA = rectus abdominis muscle; RF = rectus femoris muscle; TE/LE = thoracic and lumbar extensor muscles

Introduction
Preterm infants have a higher risk for the development of motor dysfunctions than babies born at term. The motor dysfunctions range from the various forms of cerebral palsy to minor motor disabilities (Escobar et al., 1991; Ornstein et al., 1991) which vary with age. During infancy, minor dysfunctions especially are found in the regulation of muscle tone (‘transient dystonia’). The muscle tone dysregulation mainly affects the axial muscles and results in a hyperextended posture of neck and trunk (Drillien, 1972; Touwen and Hadders-Algra, 1983; De Groot et al., 1992). At school-age and during adolescence the most consistently reported minor dysfunctions are abnormalities in postural control and balance, co-ordination problems, and a poor quality of gross and fine movements (Hadders-Algra et al., 1988; Largo et al., 1990, Soorani-Lunsing et al., 1993; Olsen et al., 1997). Pre- and perinatal brain lesions play a role in the genesis of the major and minor motor dysfunctions, but the relationship between the documented lesions and the functional outcome is not a simple one. Periventricular leukomalacia and haemorrhagic parenchymal lesions are associated with a high risk for the development of cerebral palsy, but not all infants with these types of brain lesion do develop a neurological handicap, nor can infants without such lesions be considered as free from risk for cerebral palsy (De Vries et al., 1985; Fazzi et al., 1994; Rademaker et al., 1994). Likewise, an association has been found
between the duration of periventricular echo densities and the development of minor neurological dysfunction (Jongmans et al., 1993), but children can also develop minor motor dysfunction in the absence of abnormal ultrasound or MRI scans of the brain (Roth et al., 1993; Weisglas-Kuper et al., 1994; Olsen et al., 1997).

Deviant postural control can be considered as one of the key dysfunctions in the major and minor motor abnormalities of preterm children. Therefore, we decided to study the relationship between brain lesion, neurological outcome and postural control in children born before term age. Postural control is a task of reputed complexity, as the nervous system has to deal with a redundancy in degrees of freedom due to the multitude of participating muscles and joints. Bernstein (1935) suggested that the motor problem posed by the surplus in degrees of freedom, can be solved by organizing motor output with the help of synergies. These enable the nervous system to reduce the number of afferent signals needed to generate and guide an ongoing movement and to reduce the number of efferent activities involved in motor control. This means that the brain does not need to specify each single muscle contraction, but can have access to neuronal representations of movements with prestructured motor commands. The nervous system indeed organizes postural control with the help of synergies/flexible synergies, which can be fine-tuned to task-specific conditions (Horak and Nashner, 1986; Keshner et al., 1988; Hirschfeld and Forssberg, 1991; Allum et al., 1993; Macpherson, 1994).

Forssberg and Hirschfeld (1994), who studied postural adjustments in sitting adults, formulated a functional model on the organization of postural adjustments—the so-called central pattern generator model. In general, central pattern generator activity is used to describe the neural organization of rhythmical movements like locomotion, respiration and mastication. The central pattern generators refer to neural networks co-ordinating the activity of many muscles. The activity level in these networks is controlled by reticulospinal networks co-ordinating the activity of many muscles. The generator activity is used to describe the neural organization of rhythmical movements like locomotion, respiration and mastication. The central pattern generators refer to neural networks co-ordinating the activity of many muscles. The activity level in these networks is controlled by reticulospinal neurons, whereas segmental afferent input results in modulation of the output pattern (Grillner et al., 1995). Essential to the central pattern generator model for postural adjustments is its organization in two levels. The first level is involved in the generation of the basic direction-specific response pattern. Direction-specificity means that perturbations inducing a forward sway of the body elicit a response pattern in the muscles on the dorsal side of the body, while perturbations inducing a backward body-sway evoke responses in the ventral muscles. In sitting adults, somatosensory information generated by pelvis rotation triggers the activity of the direction-specific muscles. The second level is involved in the fine-tuning of the basic response pattern on the basis of multisensory afferent input from somatosensory, visual and vestibular systems. This modulation can be achieved in various ways, for instance, by changing the order in which the agonist muscles are recruited (e.g. in a caudo-to-cranial sequence or in the reverse order), by modifying the size of the muscle contraction (EMG amplitude) or by altering the degree of antagonist activation.

In a recent series of ontogenetic studies we demonstrated that three phases can be distinguished in the normal development of postural adjustments during sitting (Hadders-Algra et al., 1996a, 1998). The first phase is the primary variability phase, which is characterized by a large variation in direction-specific postural response patterns. The variation is especially noticeable in the combinations in which the postural muscles are activated. During this phase, which starts at ‘pre-sitting’ age, postural adjustments cannot be adapted to task specific conditions. At the end of the first phase, around 9–10 months, the response pattern including all direction-specific muscles (the ‘complete’ pattern) is selected, a process resulting in a decrease in response variation. The second phase is the transient toddling phase, which occurs between 9–10 months and 2½–3 years. It is characterized by an invariant use of the ‘complete’ direction-specific response patterns and a relatively high amount of antagonist activation. These high-energy demanding postural adjustments can be adapted to task specific conditions, such as various sitting positions or different velocities of the perturbation. During this phase the focus of adaptation lies close to the support surface, i.e. it affects especially the caudally located muscles. The third phase is the secondary variability phase, during which the variation in the direction-specific response patterns returns. The postural adjustments are less energy demanding and consist of a variable activation of agonistic and antagonistic postural muscles. Task specific modulation is realized in a different way than during the previous phase, as the focus of adaptation is now located in the neck muscles. This phase starts at 2½–3 years and continues into adulthood, with further refinements in adaptational abilities occurring with increasing age (cf. Berger et al., 1985, 1995).

In the present study we assessed postural adjustments during sitting on a moveable platform in three groups of children, aged 1½–4½ years: a group of preterms, whose neonatal ultrasound scans of the brain showed distinct periventricular white matter (PWM) pathology, a group of preterms with normal ultrasound brain-scans and a group of healthy children born at term. The following questions were addressed. (i) Do PWM lesions result in (a) an absence of the direction-specificity of postural adjustments or, in case direction-specific postural adjustments are present, a dominance of the response pattern, in which all direction-specific muscles participate (the ‘complete’ response pattern), beyond the age of 2½–3 years, (b) an increased activation of antagonist muscles as a simple solution to cope with postural instability, (c) a delayed activation of the postural muscles, and (d) a deficit in the ability to modulate the EMG amplitude of the postural muscles? (ii) Do the abnormalities in postural adjustments during platform perturbations correlate better with findings at the neurological examination than with the site or the size of the PWM lesions? (iii) Does preterm birth itself affect the development of postural adjustments?
Table 1 Characteristics of preterm infants

<table>
<thead>
<tr>
<th></th>
<th>With brain lesions PWM group</th>
<th>Without brain lesions PT control group</th>
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<tbody>
<tr>
<td>Age at assessment (years)</td>
<td>1.5–4.5 (median 3)</td>
<td>1.5–4.5 (median 3)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/4</td>
<td>9/4</td>
</tr>
<tr>
<td>Gestational age at birth (weeks)</td>
<td>25–34 (median 28)</td>
<td>25–34 (median 28)</td>
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<tr>
<td>Birthweight* (g)</td>
<td>707–1463 (median 977)</td>
<td>780–1135 (median 1135)</td>
</tr>
<tr>
<td>Small-for-gestational age (n)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory distress syndrome* (n)</td>
<td>8</td>
<td>4</td>
</tr>
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*Mann–Whitney: no significant difference between the two groups.

Methods

Subjects

Three groups of 13 children, with ages varying from $1\frac{1}{2}$ to 4 years, were assessed: two groups of preterm children and one group of children born at term. The preterm children were members of the Stockholm Neonatal Project, in which series of infants with a birthweight $\geq 1500$ g were admitted to the neonatal unit of the Karolinska Hospital in Stockholm during the period September 1988 to February 1993 (Lagercrantz et al., 1997). We selected from this series all surviving children with distinct PWM lesions on the serial neonatal ultrasound scans of the brain (Hesser et al., 1997). This resulted in a study group of 13 children (PWM group), whose ultrasounds either showed PWM lesions graded as W3 (periventricular germinal matrix and in the ventricles) or W4 (large, intense echo densities extending into the deep layers of the white matter—including cases which in the Papile classification system (Papile et al., 1978) would have been categorized as grade IV haemorrhages]). Seven children of the PWM group exhibited signs of haemorrhages in the periventricular germinal matrix and in the ventricles (Table 2). For each PWM child we selected two control subjects: (i) a preterm control from the Karolinska cohort with a normal neonatal ultrasound scan of the brain, who was matched to the PWM child with respect to gestational age at birth, birthweight, sex and age at follow-up (pre-term control group), and (ii) a healthy full-term child, matched to the PWM child for sex and age at follow-up (full-term group). Details on the characteristics of the preterm children are listed in Table 1.

The children born at term were recruited among acquaintances of the investigators. They had a birthweight which was appropriate for their gestational age and they were free from developmental dysfunction. All parents gave informed consent and the procedures were approved by the medical ethical committee of the Karolinska Hospital. Prior to each assessment on the platform, one of the investigators (M.H.A.), who was ‘blind’ with respect to the group membership of the children, assessed neuromotor development by means of Hempel’s examination technique (Hempel, 1993). This examination technique is largely based on a standardized, free field observation of spontaneous motor behaviour and pays special attention to the presence of minor neurological dysfunction. We also recorded the body length and body weight of the children.

Experimental design

The protocol, recording and analyses techniques were similar to those described in Hadders-Algra et al. (1996a). The procedures were as follows.

Protocol

The children sat on a moveable flat platform, which produced a standard series of 32 random forward and backward translations with an amplitude of 6 cm. It turned out that one child was unable to sit independently. He was supported by the experimenter. Shortly before the trial the support was withdrawn, ensuring that the child was freely sitting during the perturbation. Immediately after the trial, his support was re-established. The support-withdrawal-support procedure was also used in the study of ‘non-sitting’ infants and turned out to produce a body-sway in the direction opposite to the platform translation (Hadders-Algra et al., 1996a). A standard block of trials consisted of 16 slow perturbations (forward: 120 mm/s, 500 ms duration; backward: 180 mm/s, 333 ms duration), followed by 16 fast ones (forward: 180 mm/s, 333 ms duration; backward: 220 mm/s, 272 ms duration), stimuli that were well tolerated by young children. A higher platform velocity was chosen for backward than for forward translations because of the different response threshold for the two situations (Forssberg and Hirschfeld, 1994). The forward and backward trials were presented in a random order, with a variable inter-trial interval of about 8–10 s.

EMG and kinematic recordings

Surface EMGs were recorded from the sternocleidomastoides [neck flexor (NF)], rectus abdominis (RA), rectus femoris (RF), neck, thoracic and lumbar extensor muscles (NE, TE and LE) and hamstrings (HAM) on the left side of the body. TE and LE were analysed together (TE/LE), as they were usually activated in concert.

Additionally, we were able to record kinematics simultaneously with the EMGs in five of the PWM children, eight of the preterm control children and five of the full-term
children. The kinematic data were recorded by an ELITE system in a two camera configuration for 3 s, starting 1 s prior to perturbation. Reflective markers were put on the left side of the body (i) on the caput mandibulae, (ii) 1 cm in front of the angulus mandibulae, (iii) on the anterior superior iliac spine, and (iv) on the trochanter major. Additionally, three markers were put on the lateral side of the platform. Off-line data processing consisted of the calculation of spatial angles for the head (by a vector between markers 2–1), the pelvis (markers 4–3) and the body sway (markers 4–1) in relation to the horizontal axis. The ELITE data frequently were incomplete, because the two camera systems often lost track of a marker due to arm movements or slight rotations of the head.

Data acquisition and analysis

EMG analysis. The signals from the platform and the EMGs were sampled at 800 Hz, digitized at 12-bit resolution and stored on SC/ZOOM, a dedicated signal analysis computer system (Department of Physiology, Umeå University, Sweden). The software program converted the signals to root mean square with a 6 ms moving window averaging technique. A graphics terminal was used to define interactively EMG events for each trial separately. The interactive assessment offered the possibility to differentiate EMG bursts from regularly occurring electrocardiac activity, which especially was present in RA. EMG base-line activity was defined as the mean activity recorded 500 ms prior to each perturbation. A perturbation related EMG burst was considered to be present when, during the time the platform moved, a burst occurred lasting at least 30 ms and exceeding base line activity by 2 SD. Likewise EMG inhibition was defined as a drop of activity below 1.5 SD of the baseline level, which lasted for at least 30 ms.

The first step in the analysis consisted of the documentation of muscle activation patterns by describing the presence of bursts and inhibition in the recorded muscles. This resulted for each child in each condition (forward-slow, forward-fast, backward-slow, backward-fast) in rates of EMG events per muscle and rates of muscle activation patterns. The response rates were calculated for each child and each condition by dividing the number of trials with a response by the total number of trials. Response rates were calculated for the direction-specific agonist muscles and for the antagonist muscles. The activity of the direction-specific agonist muscles was also expressed in patterns of muscle activation, i.e. in the combinations in which agonists were activated in concert (see Fig. 4). This resulted in a response rate of specific patterns and in a pattern variation index (number of different patterns divided by the number of trials).

The next step consisted of the analysis of EMG amplitudes and latencies. Latencies were defined as the time-interval between the onset of platform movement and the onset of an EMG response. In order to be able to compensate for the age-dependent changes in body-size, absolute latencies were also transformed into relative latencies by dividing latencies (in milliseconds) by body length (in metres). Amplitudes were computed by calculating the mean amplitude during a period of 100 ms and 400 ms, respectively, starting at the onset of the first burst belonging to the postural response. The baseline activity was subtracted from these ‘raw’ mean amplitudes values. The amplitude during the 100 ms period reflects the power of muscle activation during the early phase of the response, whereas the amplitude during the 400 ms period represents the overall activity, including the activity based on long latency processes of presumed transcortical origin (Marsden et al., 1983; Palmer and Ashby, 1992). Mean latencies and amplitudes were calculated for each child in each condition separately. The effect of platform velocity on EMG amplitude was expressed by means of an EMG velocity ratio consisting of the ratio between mean EMG activity during fast translations and that during slow translations.

The effect of brain lesions was evaluated with help of the matched pairs design allowing for the use of the Wilcoxon test. For the analysis of within-group differences (e.g. type of brain lesion in preterm children, type of neurological condition at follow-up) and the differences between all preterm and full-term children the Mann–Whitney test was used.

Kinematic analysis. Focus was on the angular values at movement onset and the angular displacements (the difference between peak value and onset value) of head, pelvis and body sway. Pearson’s correlation coefficient was used for the calculation of correlations between initial sitting position and angular displacement on the one hand and muscle activity on the other hand. Before entering the angular values at movement onset and the EMG amplitudes into the correlations, the data were normalized. The initial angles were normalized by subtracting the child’s mean initial angle from the actual trial’s value. The EMG amplitudes were normalized with respect to the maximal amplitude (100%) produced by the child in the relevant muscle and time-window.

Throughout the study differences and correlations where $P < 0.05$ were considered to be statistically significant. For brevity’s sake only the data during the fast translations will be reported, unless there is a special need for the data during the slow trials (e.g. in the evaluation of a platform velocity effect).

Results

Neurological outcome

Only one of the preterm children with a PWM lesion had no neurological dysfunctions at follow-up. Nine children of the PWM group showed minor neurological dysfunction and three had developed a cerebral palsy, each of them a different form: a spastic diplegia, a spastic hemiplegia and a spastic tetraplegia with mental retardation and epilepsy. The children with the diplegia and hemiplegia were able to walk without
with spastic tetraplegia, who was unable to sit without help (Figs 2 and 3). He showed no responses during forward translations. During backward translations he reacted with an occasional weak activation of the direction specific dorsal muscles, most frequently of the NE (36% of the trials), which was followed by a late and clear response in the ventral muscles.

The activation rates of the individual direction-specific agonist muscles during forward and backward translations did not differ between the three groups. A difference was, however, present in the rate of extensor inhibition during forward translations. Such an extensor inhibition is in young children part of the response pattern during forward translations, but with increasing age extensor inhibition gradually disappears (Fig. 2). Extensor inhibition occurred in the present full-term children older than 2\(\frac{1}{2}\) years in 12% of the trials (median value). When excluding the non-responding tetraplegic child, the rate of extensor inhibition was 90% in the group of children with PWM lesions over 2\(\frac{1}{2}\) years, indicating a significant difference with the full-term group (Wilcoxon, \(P < 0.05\)). The rate of extensor inhibition in the preterm control group fell in between that of the other two groups (62%), thereby showing no statistically significant difference with either.

Besides the response rates of the individual agonist muscles, we also evaluated the way in which the agonists were activated in concert. This resulted in a large variety of response patterns (Fig. 4).

None of the patterns during forward or backward translations occurred more often in a specific group of children. This also held true for the patterns in which all agonists participated (NF + RA + RF and NE + TE/LE + HAM, respectively), patterns which are known to show developmental changes (Hadders-Algra et al., 1998). Still a remarkable difference was found between the PWM and control groups in the response patterns during forward translations. The difference was found in the variation of the patterns within an individual child (Fig. 4). The response variation during forward translations was significantly lower in the PWM group than in both control groups, as was reflected by a significant difference in the pattern variation index (Fig. 5). The pattern variation index was related to the presence of a PWM lesion, but not to its severity. Neither did the pattern variation index show a relationship with the neurological condition at follow-up. The pattern variation index during backward translations did not differ between the three groups.

**Antagonist muscle activity**

During normal development antagonistic muscle activity is transiently present between 9 months and 2\(\frac{1}{2}\)–3 years, especially during forward translations (Hadders-Algra et al., 1998). All full-term and the majority of preterm children followed this developmental pattern of antagonist activity. Two children were an exception to this general rule: the child

**Direction-specific muscle activity**

Forward and backward translations of the platform induced a sway of the body in the opposite direction in all children. All but one of the children were able to maintain balance during the platform perturbations. They showed direction-specific postural adjustments, consisting of a preference for the activation of the ventral muscles during a backward sway of the body and a primary activation of the dorsal postural muscles during a sway of the body in the opposite direction (Figs 2 and 3).

This basic level of postural control was absent in the child

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with spastic diplegia (3 years old) and the child with spastic hemiplegia (3 years). Two children showed considerable antagonist activity during forward translations, with NE, TE and HAM showing a response in at least 50% of the trials (in the hemiplegic child on both sides of the body). They also showed unusual antagonist activity during backward translations. In the diplegic child this antagonist activity was restricted to the leg muscles (RF was activated in 30% of the trials), whereas in the hemiplegic boy, the antagonist activity occurred bilaterally from leg to neck (RF 100%, RA 80%). The pattern of antagonist activity was variable in all groups, with a pattern of co-activation prevailing in the neck and leg muscles, and a pattern of reciprocal activity dominating the trunk muscles.

**Timing of agonist activity**

Up until 2 years of age, the relative latencies to agonist activation during forward and backward translations decrease significantly with increasing age. The latencies are not affected by the velocity of the perturbation (Hadders-Algra et al., 1998) (Fig. 6). All children of the full-term and preterm control groups had age-appropriate response latencies, while the relative latencies of the children in the PWM group, who were older than 2 years, were considerably shorter than those of the full-term group [during forward translations: NE, $P = 0.04$; RA, $P = 0.09$ (ns); RF, $P = 0.01$; during backward translations: NE, $P = 0.01$; TE, $P = 0.07$ (ns); HAM, $P = 0.14$ (ns); Fig. 6]. The relative latencies were not related to either the severity of the PWM lesion or the neurological condition at follow-up. The finding of reduced latencies in children with significant brain lesions was supported by the presence of a significant asymmetry in the latencies in the child with spastic hemiplegia. The latencies on the affected side of his body were significantly shorter than those on the unaffected side [paired $t$ test, differences during forward translations: NF, $P < 0.01$; RA, $P = 0.19$ (ns); RF, $P < 0.01$; during backward translations: NE, $P < 0.05$; TE, $P = 0.38$ (ns); HAM, $P < 0.01$].

The sequence in which the agonistic muscles were recruited during forward and backward translations showed considerable variation in all groups. The order of muscle recruitment was not clearly related to the presence or the severity of a PWM lesion, preterm birth or the neurological condition at follow-up.

**Modulation of agonist EMG amplitude**

From 9 months onwards children can modulate the EMG amplitude of the agonistic ventral muscles during forward translations with respect to platform velocity: a higher platform velocity results in a moderate, but significant increase of the EMG amplitudes (Hadders-Algra et al., 1996a, 1998). All children in the present study (except for the child with the tetraplegia) showed this modulating capacity. Remarkably, from the age of 2 years onwards, the velocity effect turned out to be stronger in the preterm children than in the full-term children. This difference in sensitivity to platform velocity was reflected by significantly higher velocity ratios of $RA_{100}$ and $RF_{100}$ (the mean amplitudes over the first 100 ms of the response) in the preterm than in the full-term children (Fig. 7). The higher velocity ratios were found in both groups of preterm children, indicating that this effect was not related to the presence of PWM lesions, but to the preterm birth itself. Within the preterm children the velocity ratios were not related to gestational age at birth, birthweight or neurological condition.

In none of the children without cerebral palsy, nor in the...
Postural adjustments in preterm children

Fig. 2 Response patterns during forward translations. Average activity during eight fast translations. Note the absence of extensor inhibition in the full-term (FT) child of 4 years, the brisk agonist activity and extensor inhibition in the preterm (PT) children (all from the PWM group), the antagonist activity in the diplegic and hemiplegic child and the absence of response activity in the tetraplegic child (single trial). MND–A = minor neurological dysfunction–awkward; MND–B = minor neurological dysfunction–block; PLF = platform displacement; NF = neck flexors; NE = neck extensors; RA = musculus rectus abdominis; TE = thoracic extensors; LE = lumbar extensors; RF = musculus rectus femoris; HAM = hamstring muscles. Time calibration (horizontal bar): 100 ms; amplitude calibration (vertical bar): 0.4 mV.

Child with spastic tetraplegia, was a velocity effect on EMG amplitude present during backward translations, but the children with spastic diplegia and spastic hemiplegia did have such a velocity effect in the dorsal muscles. The boy with spastic diplegia showed significant velocity effects in NE100 and TE400 (paired t test: \( P = 0.02 \) and \( P < 0.0001 \), respectively) and the boy with hemiplegia demonstrated a velocity effect bilaterally in TE400 and HAM100 (paired t test: \( P < 0.01 \) and \( P = 0.02 \), respectively) and on the unaffected side in NE100 (paired t test: \( P < 0.001 \)).

From 9 months onwards children are also able to modulate EMG amplitude during forward translations with respect to sitting position. The modulating effect is brought about by initial pelvis position. Until about 3 years of age initial pelvis position affects the amplitude of RF; in older children the effect moves to NF (Hadders-Algra et al., 1996a, 1998). In both groups of preterm children this modulating capacity was totally absent (Fig. 8).

None of the full-term and preterm children showed during the present perturbation procedure, which consisted of two series (a slow series and a fast series) of randomly distributed forward and backward translations of a similar amplitude, signs of central ‘set’ or adaptation due to prior experience (cf. Horak et al., 1989).

Discussion
The present study revealed that the neural control of postural adjustments in preterm children differs from that of age-matched children born at term. Some of the postural...
dysfunctions were related to neonatal PWM lesions, others to preterm birth itself. The presence of a PWM lesion was not only associated with the development of neurological dysfunctions, but also to deficient spatial and temporal characteristics of the postural responses. Preterm birth affected the ability to modulate the EMG responses. During forward translations preterm children showed a higher sensitivity to platform velocity than full-term children, but they lacked the capacity to modulate EMG amplitude with respect to initial sitting position.

**Postural dysfunctions related to PWM lesions**
Serious PWM lesions can result in a severely handicapping condition, in which the subject cannot sit without help. One of the children of the present PWM group developed such a condition. His postural adjustments showed a profound deficit: he did not show distinct direction-specific responses, indicating that he lacked control at the basic level of postural organization (cf. Forssberg and Hirschfeld, 1994). The absence of direction-specificity cannot be attributed to the inability to sit without help, as ‘non-sitting’ infants of 5–6 months do exhibit significant direction-specificity (Hirschfeld and Forssberg, 1994; Hadders-Algra et al., 1996a). However, the reverse is probably true: it is unlikely that children who lack direction-specific postural responses develop the ability to sit independently. Two explanations can be offered for the absence of direction-specific responses: (i) the circuitries producing the basic muscle patterns, i.e. the synergies, have not developed, and (ii) the sensory pathways were not sufficiently integrated to elicit activity in the synergies.

Variation is a primary property of normal neurological
Fig. 4 Distribution of response patterns during fast forward translations in the full-term (FT) and the preterm (PT) PWM group. Each horizontal bar represents the distribution of response patterns for one subject. The PWM group is ranked according to the severity of the neurological condition at follow-up; the age-matched FT control subjects are displayed on the same horizontal level as the PWM subjects. N = neurologically normal; MND = minor neurological dysfunction; MND-H = MND with mild hypotonia; MND-B = MND-block; MND-A = MND with awkward motility; CP-HE = cerebral palsy with spastic hemiplegia, A denoting the affected side and U the unaffected side; CP-DI = spastic diplegia; CP-TE = spastic tetraplegia. The explanation of the colour-codes is given in B. In this panel hatching of a square indicates participation of a muscle in a particular pattern. The unusual diagram should be read as follows. Take for instance, the first (upper row) child of the PWM group, who was exposed to eight fast translations. She responded during one trial with NF \( \text{RA} \), (12.5% black hatching), during three trials with the combination of NF \( \text{RA} + \text{RF} \) (37.5% dark green shading) and during four trials she responded with the combination of extensor inhibition and NF \( \text{RA} + \text{RF} \) activation (50% red shading).

Development, including the development of postural control (Touwen, 1978; Forssberg, 1985; Edelman, 1989; Hadders-Algra et al., 1998). A rich variation at an early age allows the selection of the most appropriate response pattern, which, as a result of following developmental processes, can be adapted to task specific constraints (Hadders-Algra et al., 1996a). Possibly, substantial variation in postural responses, offering the possibility of selection of the best response, is a prerequisite for the development of the ability to modulate postural activity. This suggestion is supported by the present study: the children with a PWM lesion showed a reduced variation in postural responses, and an inability to modulate their postural adjustments with respect to the initial sitting position. Others also noted that a lack of variation, reflected by the presence of monotonous and stereotyped motor behaviour, is an early marker of an abnormal neurological development (Touwen, 1978; Hadders-Algra et al., 1997). Moreover, a similar lack of variation has been reported for postural adjustments of children with spastic diplegia (Brogren et al., 1998).

Animal research demonstrated that early brain lesions induce complex types of reorganization, the type depending on the site and the size of the lesion and the subject’s age at the insult (Kolb and Whishaw, 1989). Undamaged parts of the brain can take over functions of the lesioned parts, but this may be at the expense of the quality of other functions served by the hosting tissues (Huttenlocher and Raichelson, 1989; Kolb and Whishaw, 1989). The limited data available on neural reorganization after early brain damage in humans confirm the presence of complex patterns of reorganization, such as the possibility of functional compensation by undamaged parts of the brain (Brouwer and Ashby, 1991; Carr et al., 1993). Our data corroborate the idea of complex reorganization: in all but one of the children with a PWM lesion the basic level of postural control had developed, albeit with the help of seemingly simplified neural circuitries.
containing fewer interneuronal connections. Such simplified circuitries would generate little variation in the output patterns, and require relatively little processing time. This is exactly what we found in the children with a PWM lesion: less variation in the postural responses and shorter latencies until response onset.

The shorter latencies (with a reduction in absolute values of ~10 ms) seem to be at variance with the common finding of longer latencies to various responses in children with brain dysfunction. Two factors might explain the discrepancy. First, differences in the type of the evaluated responses might play role, e.g. visual or somatosensory evoked potentials or cutaneomuscular reflexes (Evans et al., 1991; Cooke, 1992; Taylor, 1992) versus postural adjustments in the present study. Secondly, the age of the subject appears to be an important factor. The majority of studies reporting longer latencies to responses in children with brain dysfunction (e.g. latencies to somatosensory or visual evoked potentials) have been performed during the first year of life (Cooke, 1992; Taylor, 1992). Also in the present study the younger children tended to have increased latency values, whereas only after the age of 2 years were the shorter latencies found (Fig. 6). This might imply that certain developmental processes in the nervous system should have occurred (see Hadders-Algra et al., 1998) before short-for-age latencies to motor responses in children with brain-damage can be found. This, in turn, could explain why others, who looked for longer latencies in sensorimotor responses of children with brain dysfunction, failed to find unequivocally longer latency values (Evans et al., 1991; Muller et al., 1992). The short-for-age latencies could be due to altered polysynaptic spinal pathways induced by the early damage of the brain (cf. Berger et al., 1985; Harrison, 1988; Hadders-Algra, 1993; Myklebust and Gottlieb, 1997).

The children of the PWM group showed more extensor inhibition during forward translations than the control children, slightly more than the preterm controls and significantly more than the full-term controls. A prerequisite for the manifestation of extensor inhibition in the EMG recordings is a relatively high tonic background activity in the dorsal extensor muscles (Hadders-Algra et al., 1996a). This indicates that the preterm children, and especially those with a PWM lesion, had a significantly higher tonic activity in their neck and back muscles. It is conceivable that this relatively high tonic activity in the extensor muscles is an expression of the same pathophysiological condition which, at earlier ages, produces the posture of hyperextension of neck and trunk so characteristic of many preterm infants (Drillien, 1972; Touwen and Hadders-Algra, 1983; De Groot et al., 1992).

The majority of children with a PWM lesion did not differ from the control children in the amount of antagonistic co-activation. An excessive amount of antagonistic co-activation was only found in the two children with a moderate form of cerebral palsy, which is in agreement with findings of others on postural control in children with spastic cerebral palsy (e.g. Berger et al., 1984, 1985; Brogren et al., 1996, 1998; Woollacott et al., 1998). The excessive co-activation can be regarded as a primary dysfunction, based on altered intra- and supra-spinal circuitries due to the early brain lesion (Leonard et al., 1991a; Myklebust and Gottlieb, 1997), or as a secondary phenomenon, as it could serve also as a functional compensation for the postural instability inherent to cerebral palsy (Woollacott et al., 1998). The finding of equal amounts of co-activation on both sides of the body in the boy with spastic hemiplegia might be an argument in favour of the latter explanation.

The present study revealed that PWM lesions are related to significant postural dysfunctions in the age period of 1½-4½ years. Whether or not the dysfunctions remain present at older age needs to be determined. For the children with cerebral palsy, it seems likely that the postural problems persist, as EMG studies on the development of locomotor behaviour in these children with cerebral palsy indicated that the basic motor deficits do not change with increasing age (Berger et al., 1984; Leonard et al., 1991b). Whether the same holds true for the children with minor neurological dysfunction is less clear, as the expression of minor neurological dysfunction changes substantially between toddler age and adolescence (Hadders-Algra and Touwen, 1999).

**Postural dysfunctions related to preterm birth**

Preterm birth was associated with an altered capacity to modulate EMG amplitude during forward translations. First, preterm children showed a higher sensitivity to platform velocity than children born at term. This could point to a
higher velocity sensitivity of muscles to stretch, analogous to that of spastic children, which has been attributed to changes in the intraspinal circuitry, such as low degree of presynaptic inhibition of the muscle spindle afferents (Crenna, 1998).

Secondly, preterm children lacked the ability to modulate EMG amplitude with respect to initial sitting position. Normally, this ability develops at 9–10 months (Hadders-Algra et al., 1996a), indicating that from this age onwards, infants have access to complex postural control mechanisms consisting of three basic components: (i) afferent information on the orientation of body segments, including the information from load receptors (cf. Berger et al., 1995), and the position of the centre of gravity; (ii) an internal postural reference frame; and (iii) postural motor output (Massion, 1994). Training experiments demonstrated that daily balance practice accelerates the development of the modulating ability by 2 months (Hadders-Algra et al., 1996b), suggesting a role of experience and learning. The inability of preterm children to modulate the postural adjustments with respect to the sitting position can be the result of dysfunction in any of the three basic components. Considering the fact that preterm children are at substantial risk for the development of learning disorders (Hille et al., 1994), it can be hypothesized that their inability to modulate postural responses to initial sitting position is the result of a deficient capacity to learn from prior experience. More specifically, this might point to a dysfunction in the cerebellum or the basal ganglia, as these systems play a particular role in the fine-tuning of motor output, including postural adjustments, to the environment on the basis of prior experience (Bloedel, 1992; Graybiel, 1995; Kimura, 1995). The better candidate of these two systems seems to be the basal ganglia, as a recent grip-and-lift study of children with unilateral brain damage revealed that, besides extensive cortical lesions, lesions of the basal ganglia were associated with disturbances in the long-lasting developmental process of the grip-lift synergy (Forssberg et al., 1999). This is in line with Graybiel’s suggestion (1995) that the basal ganglia might play a specific role in the development of new motor patterns, i.e. in the formation of...
procedural memories. In this respect it is also interesting to note that results from animal research indicated that the basal ganglia seem to be particularly vulnerable to perinatal stress, as early mild chronic hypoxia can result in long-term changes in the striatal dopaminergic system (Gross et al., 1993). Possibly, preterm birth, which is associated with a variety of perinatal stresses, such as minor hypoxic insults, can induce adverse changes in the basal ganglia which cannot be detected on the neonatal ultrasound scans of the brain.

**Concluding remarks**

The present study revealed that preterm birth is associated with two types of postural dysfunction. One is related to distinct PWM lesions and consists of a limited repertoire of response variation. The other dysfunction is not related to lesions, which can be detected on neonatal ultrasounds of the brain. It consists of a shift of postural control which is guided by feedforward processes based on prior experience, to a form of postural control which is dominated by feedback mechanisms.

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