CHAPTER 7

ASSOCIATIONS BETWEEN DEVELOPMENTAL
TRAJECTORIES OF MOVEMENT VARIETY
AND VISUAL ATTENTION IN FULLTERM AND
PRETERM INFANTS DURING THE FIRST SIX
MONTHS POSTTERM

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Provisionally accepted.
Abstract

Background
During early infancy major developmental changes, both in the variety of body movements and in visual attention, help the infant to explore its surroundings and depend on a gradual shift from subcortical to cortical functioning.

Aims
First, to determine whether preterms reach mature levels of movement variety and visual attention earlier than fullterms. Second, to determine whether individual developmental trajectories of movement variety and visual attention were associated. Finally, we compared the associations of developmental trajectories between fullterm and preterm infants.

Study design
In this longitudinal study, 20 fullterm and 9 low-risk preterm infants performed a visual disengagement task every four weeks until 6 months postterm. For each infant we drew up developmental trajectories for movement variety, and for frequencies and latencies of look. We analyzed the developmental trajectories by means of general linear model (GLM) repeated measures and Monte Carlo analyses.

Results
In comparison to fullterms, preterm infants showed a similar increase in movement variety over time ($F(4,108)=0.27; \text{partial } \eta^2=0.01; P=.90$). Visual attention reached mature levels four weeks earlier than movement variety. This effect was stronger in fullterm infants. Neither in fullterm nor in preterm infants did we find an association between the developmental trajectories of movement variety and visual attention. $P$ values ranged from .37 to .99.

Conclusions
During the first 6 months postterm, movement variety and visual attention developed independently. Temporarily, preterm exposure to the extrauterine environment led to shorter latencies of looks but it did not affect developmental trajectories of frequencies of looks and movement variety.
Introduction

Infants learn about the world by exploring their surroundings. Exploration is facilitated by infants’ ability to move their eyes from one location to another and by developing motor behaviour such as adjusting their posture and manipulating objects. Both visual exploration and motor behaviour are subject to rapid changes during the first 6 months postterm. During the first weeks, infants have difficulties shifting their gaze away from an object they are attending to, a phenomenon called ‘sticky fixation.’ At around 3 to 4 months, the frequency and speed of disengaging attention from a fixated stimulus and shifting gaze to a stimulus in the periphery increases substantially. At around 5 to 6 months adult levels are reached. By and large, motor behaviour during the first 8 to 10 weeks is a continuation of the prenatal repertoire. It is characterized by endogenously generated, complex, variable, and fluent movements, the so-called general movements (GMs). At around 9 weeks, GMs gradually change to fidgety general movements (FMs). Normal FMs are circular movements of small amplitude, moderate speed, and variable acceleration of neck, trunk, and limbs in all directions. In addition to GMs and FMs, infants display various other spontaneous movements that increase in number and variety with age. The largest increase is around 3 months when infants’ muscle power increases and they can more readily overcome the force of gravity. From 3 months onwards, several spontaneous movements are gradually replaced by voluntary, goal-directed movements. Gaze shifting and motor behaviour thus seem to follow more of less equally protracted developmental trajectories, each with a transition occurring around the age of 3 months. It is thought that the developmental changes of these functional behaviours reflect the shift from subcortical to cortical processing, as will be described in more detail below.

Spontaneous movements are generated by central pattern generators (CPG) in the brain stem and spinal cord. At approximately 3 months of age, the properties of many motor and sensory systems change to make the infant more suited to the extrauterine environment. These changes allow the infant to use environmental information to increase movement variation that is now more voluntary and goal-directed than before. The execution of voluntary movements involves subcortical-cortical circuits that connect regions of the frontal cortex (premotor areas and primary motor cortex) with the thalamus, basal ganglia, and cerebellum located subcortically.

Improvements in the ability to disengage attention and to shift gaze away from a fixated stimulus is thought to be mediated by subcortical-cortical circuits connecting several cortical regions (occipital, temporal, parietal, and the frontal eye fields in the frontal cortex) with several subcortical structures including the thalamus (more specifically the lateral geniculate nucleus), superior colliculus, basal ganglia, and the eye movement centres in the brain stem. It thus seems that some overlap exists in the subcortical-cortical circuits subserving voluntary movements and disengagement abilities. These circuits are referred to as basal ganglia-thalamo-cortical circuits since each circuit includes parts of the basal ganglia, thalamus, and frontal lobe and connecting links between these structures. Although these circuits appear to be organized in parallel, each circuit projects to a distinct area within the neurological structures comprising the circuit. Despite this anatomical segregation, it remains unclear whether these
subcortical-cortical circuits are related at a functional level. Based on the parallel nature of the basal ganglia-thalamo-cortical circuits and considering that synapses develop concurrently and at identical rates at corresponding levels of these anatomically segregated pathways,\textsuperscript{19} we hypothesized that maturational changes of these circuits occur at comparable stages during development. At a functional level this may imply that movement variety and disengagement abilities develop at similar rates.

Another intriguing question is whether additional sensory-motor experiences after preterm birth affects the development of these two functional behaviours. Very little is known about the differences in early motor behaviour between low-risk preterm and fullterm infants. The few available studies indicate that in low-risk preterm infants qualitative measures of motor development might be advanced as reflected in earlier onset of FMs\textsuperscript{20} and a temporary better quality of reaching performance at the age of 4 months.\textsuperscript{21} Quantitative measures such as the number of isolated movements per minute, however, were not different between low-risk preterm and fullterm infants until 18 weeks postterm.\textsuperscript{20} To date, it is unknown whether the additional extrauterine experiences of preterm infants affect developmental trajectories of movement variety.

Differences in developmental trajectories of disengagement between low-risk preterm and fullterm infants were described by Hunnius and colleagues. They found that temporarily low-risk preterm infants were faster in shifting their gaze away from a fixated stimulus.\textsuperscript{22} This led them to speculate that the maturation of cortical circuits involved in the preterm infants’ visual and attentional development was accelerated as a consequence of early visual experience.

The temporary accelerated development of reaching\textsuperscript{21} and disengagement\textsuperscript{22} might suggest that early extrauterine visual exposure led to a more generally accelerated development of cortical dependent processes because of additional exercise of both movements and visual exploration. In that case we would expect approximately the same accelerated development for movement variety and disengagement abilities in preterms in comparison to fullterm infants, resulting in roughly similar associations between developmental trajectories of movement variety and disengagement abilities for preterms and fullterms. By contrast, if the increase of the motor repertoire during the first 6 months postterm depended mainly on preprogrammed maturational processes, we would expect preterm infants to reach mature levels of movement variety at approximately the same postterm ages as fullterm infants. Then, the associations between development trajectories of movement variety and disengagement abilities might be different for the fullterm and preterm infants.

The first aim of this study was to determine whether preterm infants reach mature levels of movement variety earlier than fullterm infants. Second, we determined whether developmental trajectories of movement variety and disengagement abilities in the individual infant during the first 6 months postterm were associated. Finally, we compared the associations between developmental trajectories of fullterm and preterm infants.
Methods

Participants
Our study population consisted of infants who were enrolled in a longitudinal study on the
development of visual attention.22 The original fullterm group consisted of 20 infants whose
mothers were approached through childbirth education classes, midwives, or gym classes
between 2000 and 2002. Exclusion criteria were a gestation period <37 or >42 weeks, a birth
weight below 2800 g, and a history of prenatal and/or perinatal complications. The original
preterm group consisted of 10 infants born below 32 weeks gestation who had been admitted
to the University Medical Center Groningen between 2000 and 2002. Exclusion criteria were risk
factors for abnormal neurological development, such as prolonged ventilation (>14 days), severe
haemorrhagic and ischaemic brain lesions, and serious infections. Infants with retinopathy of
prematurity (ROP) more severe than grade 1 were also excluded.

Clinical variables were collected from medical charts (preterms) or provided by the mother.
Results of cranial ultrasound were graded using the system described by Papile et al.23 and de
Vries et al.24 The perinatal characteristics of the preterm group are shown in Table 1.

Table 1. Perinatal characteristics of the preterm group.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fullterms (N=20)</th>
<th>Preterms (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (boys/girls)</td>
<td>8/12</td>
<td>5/4</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>40.5 (37.0−42.6)</td>
<td>28.7 (27.3−32.0)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3363 (2880−4100)</td>
<td>1060 (640−2035)</td>
</tr>
<tr>
<td>IUGR (P&lt;10)</td>
<td>0 (0%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Apgar score at 5 minutes</td>
<td>8 (1−9)</td>
<td></td>
</tr>
<tr>
<td>Late-onset sepsis (positive blood culture)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Retinopathy of prematuritya</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>BPD (O₂ at 36 weeks PMA)</td>
<td>3 (33%)</td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation (days)</td>
<td>4 (1−13)</td>
<td></td>
</tr>
</tbody>
</table>

Cerebral pathology

| None                           | 3 (33%)          |
| PVE >7 days                    | 3 (33%)          |
| Mildb                          | 3 (33%)          |
| Severec                        | 0 (0%)           |

Data are given as median (minimum−maximum) or numbers (percentage). IUGR, intra-uterine
growth restriction; BPD, bronchopulmonary dysplasia; PMA, postmenstrual age; PVE, periventricular
echodensities. Empty boxes indicate that data were not available (Apgar scores) or did not apply.

aRetinopathy of prematurity stage II or worse. bMild cerebral pathology was defined as grades I and II
germinal matrix-intraventricular hemorrhage (GMH-IVH). cSevere cerebral pathology was defined as grade
III GMH-IVH, periventricular hemorrhagic infarction, posthemorrhagic ventricular dilatation (PHVD), and
cystic periventricular leukomalacia. PHVD was defined as a lateral ventricle size of >0.33 according to
Evans’ index.
**Video recording and assessment of movement variety**

Video recordings of 10 minutes of the spontaneous body movements of the infant were made during lab visits. All recordings were made during a period of active wakefulness with the infants lying in supine position. One recording was discarded because the infant was crying (Session 3). We assessed the second subcategory of the Motor Optimality List,\(^{11,12}\) age-adequacy of movement repertoire (i.e. movement variety), by counting the number of different movement patterns (maximum score of 32) observed. Previously, the interrater agreement for age-adequacy was moderate to high; the kappa statistics varying from 0.51 to 0.69.\(^{25}\) Recordings were assessed off-line by certified author MMH. In case of doubt regarding the presence of specific movement patterns, the recordings were re-evaluated together with AFB to decide on the definitive classification. A few infants showed repeated axial rolling, sat upright, or started crawling. Since the ability to roll, sit, or crawl involves cortical control, we considered these infants’ motor development as more mature than infants who had not yet reached these milestones. Therefore, we assigned these infants the maximum score observed in their group, plus one point extra.

**Measurement of visual attention in the first 6 months after birth**

Measurement sessions were conducted at 6, 10, 14, 18, 22, and 26 weeks postterm, calculated from the due date. Visual attention was tested in a disengagement task with 32 competition and 8 non-competition trials. All trials started with the appearance of a stimulus in the centre of the monitor. After the infant had fixated the central stimulus for 1 to 2 seconds, a second stimulus appeared in the periphery. While in non-competition trials the central stimulus disappeared before the appearance of the peripheral target, in competition trials the central stimulus remained when the peripheral target appeared. Competition trials thus demanded disengagement of attention and gaze from the central stimulus before an eye movement to the peripheral target could be generated. Non-competition trials did not require disengagement for gaze to shift to the newly appeared stimulus in the periphery. In the present study, we only used data from the competition trials because the improved ability of infants to disengage their attention from a fixated stimulus represented the shift of subcortical to cortical control that interested us. A detailed description of the infant testing situation and the coding of eye movements as well as a description of the same data set is described in Hunnius et al.\(^{22}\)

**Statistical analysis**

Regarding the visual attention data, we calculated the relative frequency of looks (frequency of looks divided by the number of completed trials), and the median latencies between appearance of the peripheral stimulus and the onset of an eye movement to this target per infant and session. The frequency of looks represents the ability to shift gaze towards a peripheral stimulus. The latencies of gaze shifts represent the speed of disengaging and shifting gaze towards a peripheral stimulus. We excluded the first session at 6 weeks from the analyses as there were only few data available (\(n=8\) missing). Moreover, based on the Motor Optimality List, a reliable measure of movement variety can only be obtained from 8 weeks onwards.

Thus, for each infant we drew up three developmental trajectories: one for movement variety,
one for the frequency of looks, and one for the latency of looks. To relate the developmental trajectories within individual infants we standardized the scores using the formula: $Y_{\text{norm}} = \frac{Y_{\text{obs}} - \text{min}}{\text{max} - \text{min}}$ with $Y_{\text{norm}}$ being the standardized score, $Y_{\text{obs}}$ being the observed score, and min and max being the minimal or maximal score of the 5 sessions of the individual infant. For latencies, min was the highest latency and max the lowest latency. By doing so, scores were rescaled on a one unit interval based on individual data with the value 1 representing most mature levels. Missing data on Sessions 2 or 6 would lead to inadequate standardization. Therefore, we replaced the missing data by the mean score per group on Sessions 2 and 6 before standardization. After the standardization procedure was completed, the standardized values of missing data were deleted because they only served the purpose of standardization. There were no missing data for frequency of looks on Sessions 2 or 6. Latencies were missing on Session 2 in two fullterm infants and in two preterm infants. Numbers of movements were missing in one preterm infant on Session 2, in another preterm on Sessions 2 and 6, and in one fullterm on Session 6.

Our first research question was whether preterm infants reach mature levels of movement variety and visual attention earlier than fullterm infants. The differences in the developmental trajectories of visual attention in this dataset of fullterm and preterm infants had previously been described by Hunnius and colleagues and are repeated here for the sake of completeness. The difference between the developmental trajectories of movement variety of fullterm and preterm infants was tested using GLM repeated measures with the number of observed movement patterns as within-subject variables and group as between subject factor. We replaced the missing data (Session 2 $n=2$ preterms; Session 4 $n=1$ fullterm; Session 5 $n=4$ fullterms; Session 6 $n=1$ fullterm and $n=2$ preterms) by the mean scores of movement variety on the particular sessions, separately for the fullterm and preterm group.

Our second research question was whether the individual developmental trajectories of movement variety and visual attention were associated. To take into account differences in developmental timing of movement variety and visual attention, we first examined whether developmental trajectories of movement variety or visual attention (looks and latencies) had a faster development towards mature levels using averaged curves and calculating averaged distance scores between the trajectories. For a detailed description of calculating averaged developmental trajectories of disengagement and movements see Supplement 1, Note 1. Subsequently, we examined coupling between developmental trajectories both before and after correcting for developmental timing. Coupling was defined as the difference between change scores (the difference between a score and the preceding score) of looks and movements. Coupling means that when the capacity to disengage changes to a certain extent, this is paralleled by a similar change in spontaneous movements. To prevent data loss, we used linear interpolation methods if data for Sessions 3, 4, or 5 were missing. The absolute value of the difference between change scores within an individual (i.e. similarity) was used as an indicator expressing how strongly the change in disengagement and movements were associated (the smaller the difference, the stronger they are associated). The similarity of the two trajectories in the same infant (within-subject similarity) was compared to the similarity of one of these trajectories with that of another infant (between-subject similarity) using Monte Carlo methods.
(see Supplement 1, Note 2). To maintain the longitudinal aspect of the data, the order of sessions was fixed when randomly reordering the data between infants.

For corrections in developmental timing, we used the following approach. For example, if the averaged curves revealed that movement variety reached mature levels earlier than disengagement, this would imply that the individual curves of movement variety and disengagement were not associated but that the within-subject similarity with lag 1 could eventually be greater than the similarity based on simultaneous observations (i.e. looks at time \( t + 1 \) would be more similar to movements at time \( t \) than to movements at time \( t + 1 \)). In Supplement 1, Note 3 we provide an example of the random permutation method for developmental trajectories of movement variety and looks with lag 1 for the looks (thus correcting for developmental timing). We performed these analyses for the fullterms and preterms separately so as to be able to describe differences between the two groups.

Throughout the analyses \( P<.05 \) was considered statistically significant. We used SPSS 20.0 software (SPSS Inc, Chicago, IL) for the analyses. Excel version 2007 was used for performing the Monte Carlo analyses.

![Figure 1. Development of mean number of movement patterns (A), mean frequencies of looks (B) and mean latencies of looks (C) in fullterms and preterms.](image)

Figure 1. Development of mean number of movement patterns (A), mean frequencies of looks (B) and mean latencies of looks (C) in fullterms and preterms.
Results

Movement variety and disengagement abilities during the first 6 months postterm

For the total group of infants, the median postterm ages in weeks (minimum−maximum) at the consecutive measurement sessions were: 10.4 (8.4−13.1), 14.7 (14−16.1), 18.6 (18.0−20.6), 22.6 (22.0−23.9), and 27.1 (26.0−28.1). In Figure 1, we provide the developmental trajectories of mean number of different movements and mean frequencies and latencies of looks. Our analyses revealed that movement variety, expressed as the number of different movement patterns, increased significantly over the consecutive sessions (F(4,108)=29.69; partial eta²=0.52; P<.001), but that this increase was not significantly different between the fullterm and preterm infants (F(4,108)=0.27; partial eta²=0.01; P=.90). Multivariate tests confirm that movement variety did not differ significantly between the fullterm and preterm infants over the consecutive sessions (V=0.05; F(4,24)=0.32; partial eta²=0.05; P=.86). Regarding the visual attention data, preterm infants were faster in looking at the peripheral stimulus until between 14 and 18 weeks postterm, as reported in the original study by Hunnius et al.22 Please note that we had one preterm infant less in the present study.

Developmental timing of movement variety and disengagement

In Figures 2 and 3, we present the standardized scores of mean number of different movements and mean frequencies and latencies of looks. Frequencies and latencies of looks seemed to develop faster towards mature levels than movement variety. In the fullterms, these observations were confirmed by the random permutation method based on 10,000 permutations (Table 2) for the looks (mean distance 0.137, 95% CI, 0.016−0.258, P<.001) and the latencies (mean distance 0.177; 95% CI, 0.071−0.282, P<.001). In the preterms, both frequencies of looks and latencies of looks had an almost equal development towards mature levels as movements had (mean distance 0.080, 95% CI, 0.032−0.127, P=.07 and mean distance 0.086, 95% CI, −0.071 to 0.242, P=.10). Looking in more detail at the trajectories, it seems that looks stabilized around Session 5 (22 weeks) while movements did not stabilize before Session 6 was reached (26 weeks). Post hoc, we compared change scores over Sessions 5 and 6 using the t test. In fullterm infants, looks stabilized before movements did (mean change score for looks and movements 0.003 and 0.305, respectively, P=.002) and latencies stabilized before movements (mean change score for latencies and movements 0.016 and 0.305, respectively, P=.005). In preterm infants, looks did not stabilize earlier than movements (mean change score for looks and movements 0.165 and 0.352, P=.19), while latencies did (mean change score for latencies and movements −0.079 and 0.352, respectively, P=.023).
Table 2. Mean distance scores of averaged developmental curves of movement variety and disengagement (looks and latencies) before and after random permutation in fullterm and preterm infants.

<table>
<thead>
<tr>
<th></th>
<th>Mean distance score (95% CI)</th>
<th>Mean distance score after random permutation (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>fullterms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>looks minus movement variety</td>
<td>0.137 (0.016 to 0.258)</td>
<td>0.000 (−0.062 to 0.062)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>latency minus movement variety</td>
<td>0.177 (0.071 to 0.282)</td>
<td>0.000 (−0.067 to 0.066)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>preterms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>looks minus movement variety</td>
<td>0.080 (0.032 to 0.127)</td>
<td>0.000 (−0.088 to 0.088)</td>
<td>.07</td>
</tr>
<tr>
<td>latency minus movement variety</td>
<td>0.086 (−0.071 to 0.242)</td>
<td>0.000 (−0.109 to 0.111)</td>
<td>.10</td>
</tr>
</tbody>
</table>

Distance scores are calculated as standardized scores of looks minus standardized scores of movement variety.

Figure 2. Development of mean number of movements in relation to mean number of frequencies (A) and mean latencies of looks (B), expressed in standardized scores in fullterm infants.

Figure 3. Development of mean number of movements in relation to mean frequencies of looks (A) and mean latencies of looks, expressed in standardized scores in preterm infants.
Associations between individual developmental trajectories

In Supplement 2, we provide the individual developmental trajectories of the standardized scores of spontaneous movements, frequencies of looks, and latencies of looks. Inspection of the individual curves revealed that in some infants all indexes first underwent a period of rapid change before stabilizing (see for example, fullterm infant 11 and preterm infant 5 in Supplement 2). In several other infants the indexes fluctuated considerably between the minimum and maximum values.

Our second research question was whether individual developmental trajectories of movement variety and disengagement (looks and latencies) were associated. In the fullterm infants (Table 3A), we did not find significant associations between developmental trajectories of movements and looks (mean change score 0.428, 95% CI, 0.375−0.499, $P=.51$) nor between movements and latencies (mean change score 0.473, 95% CI, 0.395−0.552, $P=.76$). Based on the averaged developmental curves, we concluded that disengagement reached mature levels earlier than movement variety. Therefore, we repeated our analyses for the individual infants with lag 1 for the looks (i.e. looks at time $t−1$ compared to movement variety at time $t$; Table 3A). Developmental trajectories of movement variety were again not associated with development trajectories of either looks (mean change score 0.435, 95% CI, 0.339−0.530; $P=.37$) or latencies (mean change score 0.488, 95% CI, 0.398−0.579; $P=.58$).

In the preterm infants (Table 3B), there were no significant associations between individual developmental trajectories of movement variety and either looks (mean change score 0.392, 95% CI, 0.290−0.495, $P=.48$) or latencies (mean change score 0.497, 95% CI, 0.397−0.616, $P=.41$). $P$ values of the averaged developmental curves ($P=.07$ and $P=.010$) showed a marginally faster development of disengagement. Therefore we repeated our analyses for the individual infants with lag 1 for looks (Table 3B). Again, no significant associations were found between developmental trajectories of movement variety and looks (mean change score 0.553, 95% CI, 0.450−0.655, $P=.99$) or between movement variety and latencies (mean change score 0.502, 95% CI, 0.361−0.644; $P=.53$).

To summarize, only in the fullterms did the frequency of looks reach mature levels around four weeks earlier than movement variety measures. Latencies of looks stabilized approximately four weeks earlier than movements in both fullterms and preterms. Individual trajectories of movement variety and disengagement were not associated in fullterms nor in preterms, neither before nor after correcting for developmental timing.
Table 3. Mean change scores of developmental curves of disengagement (looks and latencies) and movement variety before and after random permutation in fullterm (A) and preterm (B) infants.

A.

<table>
<thead>
<tr>
<th></th>
<th>Mean change score (95%-CI)</th>
<th>Mean change score after random permutation (95%-CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>movement variety−looks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no shift</td>
<td>0.428 (0.357 to 0.499)</td>
<td>0.427 (0.375 to 0.475)</td>
<td>.51</td>
</tr>
<tr>
<td>looks −4 weeks</td>
<td>0.435 (0.339 to 0.530)</td>
<td>0.445 (0.375 to 0.509)</td>
<td>.37</td>
</tr>
<tr>
<td>movement variety−latency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no shift</td>
<td>0.473 (0.395 to 0.552)</td>
<td>0.450 (0.382 to 0.509)</td>
<td>.76</td>
</tr>
<tr>
<td>latency −4 weeks</td>
<td>0.488 (0.398 to 0.579)</td>
<td>0.478 (0.390 to 0.554)</td>
<td>.58</td>
</tr>
</tbody>
</table>

B.

<table>
<thead>
<tr>
<th></th>
<th>Mean change score (95%-CI)</th>
<th>Mean change score after random permutation (95%-CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>movement variety−looks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no shift</td>
<td>0.392 (0.290 to 0.495)</td>
<td>0.395 (0.307 to 0.481)</td>
<td>.48</td>
</tr>
<tr>
<td>looks −4 weeks</td>
<td>0.553 (0.450 to 0.655)</td>
<td>0.432 (0.322 to 0.524)</td>
<td>.99</td>
</tr>
<tr>
<td>movement variety−latency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no shift</td>
<td>0.497 (0.379 to 0.616)</td>
<td>0.503 (0.404 to 0.587)</td>
<td>.41</td>
</tr>
<tr>
<td>latency −4 weeks</td>
<td>0.502 (0.361 to 0.644)</td>
<td>0.492 (0.356 to 0.609)</td>
<td>.53</td>
</tr>
</tbody>
</table>

**Discussion**

In this study we analyzed in detail the developmental trajectories of spontaneous movements, particularly movement variety, and visual attention during the first 6 months postterm in both fullterm and preterm infants. We demonstrated that movement variety increased at similar rates in preterm and fullterm infants. As was reported previously, preterms were temporarily faster in shifting their gaze away from a fixated stimulus to a peripheral stimulus. In fullterms and preterms the frequencies and latencies of looks away from a fixated stimulus to a peripheral stimulus reached mature levels earlier than movement variety, but it was strongest in the fullterms. Development of movement variety and disengagement (frequencies and latencies of looks) did not follow similar trajectories; they could not be shown to be more similar within the same infant than between different infants, not even after correcting for the differences in developmental timing. Taken together, these results suggest that movement variety and disengagement did not develop synchronously. Rather, they developed independently of one another with disengagement abilities stabilizing before movement variety.

In our cohort of fullterm and preterm infants, the number of different movements increased gradually during the first 6 months postterm with the strongest increase between 10 and 14
weeks. This is in accord with a previous study on quantitative aspects of the motor repertoire in preterm infants,\textsuperscript{11} and may be a reflection of the major neural reorganization that normally occurs around 12 weeks postterm.\textsuperscript{5} This period is characterized by a change in many neural functions to a condition more suited to the extrauterine environment: the infant’s muscle power increases and a shift from body-oriented towards space-oriented behaviour takes place. This coincides with an expanding motor repertoire including more voluntary and goal-directed movements.\textsuperscript{5}

For the ability to disengage, the steepest curves were seen between 10 and 14 weeks and between 18 and 22 weeks postterm, after which they levelled off. And again, the increase between 10 and 14 weeks might be a reflection of neural reorganization.\textsuperscript{5} Neural reorganization not only includes changes in motor systems but in sensory systems as well, as it has been shown that during this period intentional control of visual attention and binocular vision emerges.\textsuperscript{16} The increase between 18 and 22 weeks is in accord with previous studies demonstrating that disengagement abilities normally reach mature levels around 24 weeks,\textsuperscript{3,4} which suggests that by this time the cortical processes involved in disengagement are fully matured.

The question whether the additional extrauterine experience of preterm infants is beneficial or detrimental for neurodevelopment is still a matter of debate. Some researchers suggested that preterm birth may result in accelerated neural maturation\textsuperscript{26} whereas others demonstrated delayed maturation in terms of reduced cortical microstructural development.\textsuperscript{27,28} No differences in the maturation of cortical neurons between fullterm and preterm infants were also reported,\textsuperscript{29} supporting a strong genetic control of maturation of cortical neurons. The differences reported might depend partly on associated complications of preterm birth, such as cerebral abnormalities, that prevent normal brain development. In the present study we only included low-risk preterm infants, i.e. infants without major perinatal complications, which enabled us to attribute our findings mainly to earlier extrauterine exposure.

To the best of our knowledge, no previous study investigated differences in movement variety between fullterm and preterm infants. We demonstrated quite similar trajectories of movement variety for fullterms and preterms. Apparently, postmenstrual age has a greater effect on the repertoire of various movements than postnatal age, supporting the view that movement variety is largely determined by preprogrammed maturational processes rather than by the degree of postnatal sensorimotor experiences. This finding underlines previous observations by Thelen and colleagues who found that particular motor stereotypies had characteristic ages of onset that were closely associated with neuromuscular maturation as measured with the motor component of the first edition of the Bayley Scales of Infant Development.\textsuperscript{30} In support of this finding, Prechtl and colleagues demonstrated that several movement patterns were similar in blind and sighted infants alike.\textsuperscript{31} Their findings, as do ours, suggest that the expression of various motor patterns depends largely on intrinsic processes, leaving a minor role for postnatal experience. We have to keep in mind, however, that any beneficial effect of additional extrauterine experiences in preterm infants (increased freedom of movement and more opportunity to exercise) may be counteracted by a lack of adequate muscular control due to their immature state.

In comparison to fullterm infants, the shorter latencies of looks until 16 weeks postterm
in preterm infants is consistent with neuroimaging studies demonstrating accelerated cerebral
grey and white matter development at term-equivalent age in preterm infants without brain
lesions, especially in regions associated with visual processing.\textsuperscript{32,33} It seems that the additional
sensorimotor experience of preterm infants particularly enhances maturation of those pathways
that are subject to an abrupt increase in activity due to the transition from intrauterine to
extrauterine life. Whether this accelerated development has implications for later functioning
requires further study currently underway.

We found no indications for a relation between the developmental trajectories of movement
variety and disengagement abilities between 10 weeks and 6 months, neither in fullterm
nor in preterm infants. Even after correcting for the faster development of disengagement
abilities towards mature levels, we were unable to demonstrate significant associations
between developmental trajectories. This is in contrast to a previous study on simultaneous
measurements of disengagement and quantity of movements. It demonstrated that in infants
aged 1 or 3 months an increase in body movements preceded disengagement.\textsuperscript{34} The authors
speculated that an increase in general motor activation might help to unlock and redirect
gaze which aids visual exploration when the environment itself is unchanging. We offer several
possible explanations for these contrasting findings. Firstly, in their study, the authors related the
total quantity of body movements to disengagement abilities while we focused on the variety
of different movement patterns. Secondly, we measured movements and disengagement
successively to provide a measure of neurological maturation. This contrasted with the previous
study. They measured movement-attention coupling simultaneously, to provide insight into
direct functional coupling between movements and disengagement at 1 and 3 months. On
the basis of our findings we propose that the neural substrates subserving movement variety
and disengagement, which are considered to include the basal ganglia-thalamo-cortical
circuits, developed at different rates between 10 weeks and 6 months postterm – in contrast
to our hypothesis. Presumably, the anatomical segregation of the subcortical-cortical circuits
mentioned is also reflected in different maturational changes of behaviourial correlates despite
the synchronous synaptogenesis at the corresponding levels of these anatomically segregated
pathways. We must take into consideration, however, that from 3 months onwards other complex
maturational processes take place, including the formation of neural networks between several
cortical areas and selective pruning of neurons and synapses, that may have masked the parallel
emergence of functional behaviours related to these subcortical-cortical circuits.

In conclusion, we were unable to demonstrate associations between developmental
trajectories of movement variety and disengagement during the first 6 months. This suggests
that maturational changes in underlying neural substrates (basal ganglia-thalamo-cortical
circuits), developed independently. Additional exposure to the extraterine environment after
preterm birth led to faster, albeit temporary disengaging\textsuperscript{22} but it did not lead to beneficial, nor
adverse, effects on the developmental trajectories of movement variety.

The strength of our study is that we provided new insights into the development of and the
associations between two prominent early behaviours, spontaneous movements and looking,
during the first 6 months postterm. In addition, ours was the first study of its kind to examine the
effect of additional extrauterine visual exposure on these combined developmental trajectories. A limitation of this study was the relatively small study group. As a consequence, the presence of associations between developmental trajectories of spontaneous movements, i.e. movement variety, and disengagement abilities cannot be ruled out definitely.

Acknowledgements
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2. Butcher PR, Kalverboer AF, Geuze RH. Infants’ shifts of gaze from a central to a peripheral stimulus: A longitudinal study of development between 6 and 26 weeks. Infant Behav Dev 2000;23:3-21.
17. Posner MI. Orienting in normal and pathological development. Development and
ASSOCIATIONS BETWEEN DEVELOPMENTAL TRAJECTORIES OF MOVEMENT VARIETY AND VISUAL ATTENTION IN FULLTERM AND PRETERM INFANTS DURING THE FIRST SIX MONTHS POSTTERM

Supplementary material

1. Averaged developmental trajectories of disengagement and movement variety:

In order to assess which of the two developmental trajectories reached mature levels ahead of the other, we determined the distances between the standardized scores of movement variety and disengagement (looks and latencies) for each measurement within the individual infants; standardized scores looks minus standardized scores movements (Table 1). We then calculated averaged distance scores for each infant (in our example 0.156). In the example the averaged distance score is positive, implying that looks developed ahead of movement variety. In order to test the probability that the positive score could be expected on the basis of chance alone, we randomly interchanged the standardized scores of movement variety and looks of the same infant while keeping the measurement moment fixed. Our example shows that after random reordering, the average distance score is negative (−0.182). In order to determine whether the more rapid development of looks reached statistically significant levels, we carried out the random permutation procedure for all subjects simultaneously.

2. Similarities between developmental trajectories of disengagement and movement variety:

Our second research question was whether the developmental trajectories of disengagement (looks and latencies) and movement variety within the same infant were coupled. We explain the procedure with the help of an example based on standardized scores of looks and movements (Table 2).

We obtained standardized scores for each variable as described in the section on statistical analyses. For each infant we calculated change scores, defined as the difference between a score and the preceding score. The difference between the change scores of looks and movement variety is an indicator of how strongly the developmental trajectories of looks and movement variety were coupled in an individual infant (the smaller the difference, the stronger the coupling). In our example, the averaged absolute difference of change scores (last column) is 0.369. In order to obtain an estimate of the strength of the coupling between the developmental trajectories, the standardized scores of looks were replaced randomly by the standardized scores of looks of another infant, while keeping the order of measurements fixed. Table 2 provides an example of such random reordering of scores and of the resulting averaged absolute difference of change score (0.521). In this particular infant, the averaged absolute difference of change scores is greater after randomly replacing the standardized scores of looks by the standardized scores of looks of another infant, meaning that the developmental curves of the same infant were more strongly associated than the developmental curves of movement variety of one infant and the developmental curve of looks of another infant. The probability that after replacement of the longitudinal data of looks of one infant with the same data of another infant the difference scores were equally small, or smaller, than the observed difference scores is calculated by carrying out the random permutation method a great number of times, e.g. 1000 times. By carrying out a large number of randomizations, an approximation of the exact chance distribution of
the test statistic used can be obtained without having to make assumptions about expected distributions across the “population” of observations. Another advantage of permutation and resampling methods is that they are particularly suited for small datasets with missing data. The probability is calculated by comparing the observed test statistic to the test statistic that is obtained when the data are randomly assembled.

3. **Shifting developmental curves of disengagement and/or movement variety:**
To determine whether developmental trajectories were associated we had to take into account that developmental curves of looks and latencies might have stabilized before developmental curves of movement variety, or vice versa. Based on the averaged developmental curves, we repeated our analyses with shifting curves either forward or backward. In our example, we shifted the curve of looks four weeks forward (or shifting curves of movement variety four weeks backward), i.e. we determined similarities between developmental curves of looks on measurement 2–5 and developmental curves of movement variety on measurements 3–6. See Table 3 for an example. In this particular infant, the averaged absolute difference of change scores is greater after randomly replacing the standardized scores of looks by standardized scores of looks of another infant (0.400 versus 0.264), meaning that the developmental curves of the same infant were more strongly associated than the developmental curves of movement variety of that infant and the developmental curve of looks of another infant.
Table 1A. Example of differences between averaged developmental trajectories (fullterm infant 3).

<table>
<thead>
<tr>
<th>Data</th>
<th>Movement variety</th>
<th>Looks</th>
<th>Distance (looks minus movement variety)</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>t3</td>
<td>0.400</td>
<td>0.296</td>
<td>−0.104</td>
</tr>
<tr>
<td>t4</td>
<td>0.100</td>
<td>0.450</td>
<td>0.350</td>
</tr>
<tr>
<td>t5</td>
<td>0.400</td>
<td>1.000</td>
<td>0.600</td>
</tr>
<tr>
<td>t6</td>
<td>1.000</td>
<td>0.935</td>
<td>−0.065</td>
</tr>
</tbody>
</table>

0.156 (average)

Table 1B. Random permutations (looks standardized scores are randomly reordered with movement variety standardized scores of the same infant).

<table>
<thead>
<tr>
<th>Data</th>
<th>Movement variety</th>
<th>Looks</th>
<th>Distance (looks minus movement variety)</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>t3</td>
<td>0.296</td>
<td>0.400</td>
<td>0.104</td>
</tr>
<tr>
<td>t4</td>
<td>0.450</td>
<td>0.100</td>
<td>−0.350</td>
</tr>
<tr>
<td>t5</td>
<td>1.000</td>
<td>0.400</td>
<td>−0.600</td>
</tr>
<tr>
<td>t6</td>
<td>1.000</td>
<td>0.935</td>
<td>−0.065</td>
</tr>
</tbody>
</table>

−0.182 (average)

Table 2A. Example of the similarity in change in looks and movement variety term (fullterm infant 3).

<table>
<thead>
<tr>
<th>Data</th>
<th>Looks Score</th>
<th>Change</th>
<th>Movement variety Score</th>
<th>Change</th>
<th>Absolute difference change scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>t3</td>
<td>0.296</td>
<td>0.296</td>
<td>0.400</td>
<td>0.400</td>
<td>0.104</td>
</tr>
<tr>
<td>t4</td>
<td>0.450</td>
<td>0.155</td>
<td>0.100</td>
<td>−0.300</td>
<td>0.455</td>
</tr>
<tr>
<td>t5</td>
<td>1.000</td>
<td>0.550</td>
<td>0.400</td>
<td>0.300</td>
<td>0.250</td>
</tr>
<tr>
<td>t6</td>
<td>0.935</td>
<td>−0.065</td>
<td>1.000</td>
<td>0.600</td>
<td>0.665</td>
</tr>
</tbody>
</table>

0.369 (average)
Table 2B. Random permutations (looks standardized scores are replaced by looks standardized scores of another fullterm infant).

<table>
<thead>
<tr>
<th>Data</th>
<th>Looks Score</th>
<th>Change</th>
<th>Movement variety Score</th>
<th>Change</th>
<th>Absolute difference change scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t3</td>
<td>0.134</td>
<td>0.134</td>
<td>0.400</td>
<td>0.400</td>
<td>0.266</td>
</tr>
<tr>
<td>t4</td>
<td>0.279</td>
<td>0.145</td>
<td>0.100</td>
<td>−0.300</td>
<td>0.445</td>
</tr>
<tr>
<td>t5</td>
<td>1.000</td>
<td>0.721</td>
<td>0.400</td>
<td>0.300</td>
<td>0.421</td>
</tr>
<tr>
<td>t6</td>
<td>0.649</td>
<td>−0.351</td>
<td>1.000</td>
<td>0.600</td>
<td>0.951</td>
</tr>
</tbody>
</table>

0.521 (average)

Table 3A. Example of curves with lag 1 for looks (fullterm infant 3). Looks at time $t - 1$ was compared with movement variety at time $t$.

<table>
<thead>
<tr>
<th>Data</th>
<th>Looks Score</th>
<th>Change</th>
<th>Data</th>
<th>Movement variety Score</th>
<th>Change</th>
<th>Absolute difference change scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>0.000</td>
<td></td>
<td>t3</td>
<td>0.400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t3</td>
<td>0.296</td>
<td>0.296</td>
<td>t4</td>
<td>0.100</td>
<td>−0.300</td>
<td>0.596</td>
</tr>
<tr>
<td>t4</td>
<td>0.450</td>
<td>0.155</td>
<td>t5</td>
<td>0.400</td>
<td>0.300</td>
<td>0.145</td>
</tr>
<tr>
<td>t5</td>
<td>1.000</td>
<td>0.550</td>
<td>t6</td>
<td>1.000</td>
<td>0.600</td>
<td>0.05</td>
</tr>
</tbody>
</table>

0.264 (average)

Table 3B. Random permutations with lag 1 for the looks. Looks at time $t - 1$ was compared with movement variety at time $t$. Looks standardized scores are replaced by data of another fullterm infant.

<table>
<thead>
<tr>
<th>Data</th>
<th>Looks Score</th>
<th>Change</th>
<th>Data</th>
<th>Movement variety Score</th>
<th>Change</th>
<th>Absolute difference change scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>0.000</td>
<td></td>
<td>t3</td>
<td>0.400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t3</td>
<td>0.404</td>
<td>0.404</td>
<td>t4</td>
<td>0.100</td>
<td>−0.300</td>
<td>0.704</td>
</tr>
<tr>
<td>t4</td>
<td>0.380</td>
<td>−0.025</td>
<td>t5</td>
<td>0.400</td>
<td>0.300</td>
<td>0.325</td>
</tr>
<tr>
<td>t5</td>
<td>0.809</td>
<td>0.429</td>
<td>t6</td>
<td>1.000</td>
<td>0.600</td>
<td>0.171</td>
</tr>
</tbody>
</table>

0.400 (average)
Supplement 2. Individual trajectories of standardized scores of movement variety (number of movement patterns), frequency of looks and latencies.

Preterm infants:
ASSOCIATIONS BETWEEN DEVELOPMENTAL TRAJECTORIES OF MOVEMENT VARIETY AND VISUAL ATTENTION IN FULLTERM AND PRETERM INFANTS DURING THE FIRST SIX MONTHS POSTTERM

Fullterm infants:
ASSOCIATIONS BETWEEN DEVELOPMENTAL TRAJECTORIES OF MOVEMENT VARIETY AND VISUAL ATTENTION IN FULLTERM AND PRETERM INFANTS DURING THE FIRST SIX MONTHS POSTTERM
ASSOCIATIONS BETWEEN DEVELOPMENTAL TRAJECTORIES OF MOVEMENT VARIETY AND VISUAL ATTENTION IN FULLTERM AND PRETERM INFANTS DURING THE FIRST SIX MONTHS POSTTERM