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Original article

Comparative analysis of perinatal and postnatal factors, and general movement in extremely preterm infants

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Abstract

Study aim: To describe general movement in extremely premature infants and examine correlations with risk factors for antenatal, perinatal, and postnatal morbidity. *Study type:* Prospective, single-center study. Nineteen patients were followed up. *Methodology:* The infants' general movement was analyzed using video recordings. Qualitative and quantitative assessments were performed during the writhing movement (WM) period and fidgety movement (FM) period. The quality of the general movements (GMs) and the scores achieved were then correlated with antenatal, perinatal, and postnatal factors. *Results:* Infants' motor activity fluctuated during the WM period, especially in extremely premature infants where poor repertoire is often observed. No correlations were found between WMs and obstetric factors. Gestational age correlated with WMs' quality ($p = 0.023$). WMs correlated with factors of postnatal morbidity such as chronic lung disease (CLD) ($p = 0.034$) and nosocomial infections ($p = 0.05$). At 3 months corrected age, the spontaneous movement quality are correlated with neurological explorations such as US brain ($p = 0.032$), MRI ($p = 0.039$), EEG ($p = 0.036$), and neurological follow-up assessments ($p = 0.015$). *Conclusion:* Prudence must be used when performing the analysis of general movement in extremely preterm infants. WMs may be influenced by perinatal morbidity, and possibly by the severe brain immaturity of these infants. WMs correlate with CLD and nosocomial infections. Analysis of general movement in infants of 3 months corrected age is a valuable means to detect neurological disorders.

Keywords: General movement; Cerebral palsy; Perinatal factors

1. Text and aknowledgments

Improvement of perinatal care increases the chances of survival in increasingly preterm infants. However, neurological complications such as cerebral palsy or minor neurological disorders are more prevalent [1,2].

Cerebral palsy refers to a group of disorders with non-progressive motor impairment of variable semiology, resulting from brain abnormalities occurring during development. This entity is associated with varying degrees of tonus and posture disorders, as well as disorders of voluntary and automatic motor activity. Auditory and ocular disorders, visuospatial and construction dyspraxia, epilepsy, speech impairments, as well as cognitive and behavior disorders are also common [3]. Early diagnosis is essential to ensure prompt and optimal management.

Assessing the severity of neurological impairments within the first days of life and evaluating the prognosis early and in a reliable fashion are major concerns for neonatologists. This assessment currently relies on clinical follow-ups and the findings from brain ultrasonography (US), electroencephalogram (EEG), and brain magnetic resonance imaging (MRI).

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Despite advances in medical imaging, clinical follow-ups until the infant reaches the age of 1 year often represent the only way to assess the neurological impact of a history of perinatal pathology. The evaluation of passive motor activity, as described by Amiel–Tison, and the assessment of active motor activity, using the Tardieu scale, are performed by most French teams to establish the clinical diagnosis of potential cerebral palsy within the first 2 years of life.

Several studies have shown that the analysis of general movement (GMs) as described by Pretchl plays a major role in predicting, at an early stage, the neurological outcome of infants born prematurely [4–8].

Spontaneous movements are physiological fetal movements, and include different types such as startles and general movements.

GMs are endogenous and active movements, reflecting the maturing of the central nervous system. They are spontaneous movement; their repertoire is rich and complex. They display a spatiotemporal organization, and are classified into two types: writhing movements (WMs) and fidgety movements (FMs).GMs involve the whole body in a variable sequence of arm, leg, neck and trunk. They wane in intensity, force and speed and they have a gradual beginning and end. Rotations along the axis of the limbs and slight changes in the direction of movement make them fluent and elegant, and create the impression of complexity and variability. WMs are present from the fetal period to the postnatal period, approximately 2 months post-term. Normal WMs are characterized by their variability (amplitude, speed, force, and intensity), complexity (writhing movements), and fluency (involving the entire body). They dissipate progressively, being replaced by movements of the distal and proximal part of body, called FMs. The Fms appears at the time of the major neural transformation and stay until the post-term age of 20 weeks. FMs are small circular movements, with slow to moderate speed, occurring in a continuous fashion.

During the WM period, abnormal GMs show a reduced complexity, variability, or fluency. They are classified as cramp synchronized (CS), poor repertoire (PR), and hypokinetic (HK) movements. The persistence of abnormal GMs until the FM period is predictive of future neurological disorders [9].

Absent FMs permit the selection of patients at risk of cerebral palsy, with a 95% sensitivity and 96% specificity. The absence of FMs should draw the practitioners' attention to the risks of cerebral palsy, delays in motor development, or minor motor disorders [10–13].

A recent study has shown that analysis of spontaneous movement quality at 3 months corrected age (SMQ) is a good predictor of cognitive development [14]. It is the analysis of posture and competing movements, and their appearance at the correct time during development, For example pattern like kicking, hand-hand contact, hand-mouth contact, foot-foot contact, fingers movements, posture of trunk. . .and many else.

Few studies have investigated GMs in extremely preterm infants. It should be noted that neurological development is strongly influenced by antenatal, prenatal, and postnatal morbidity. Some authors hypothesize that abnormal spontaneous motor activity most often occurs in extremely preterm infants because of said morbidity, rendering its prognostic value uncertain [15,16].

This study's aims were twofold: to describe extremely preterm infants' GMs and spontaneous movement quality and also to assess correlations with antenatal, perinatal, and postnatal morbidity factors.

2. Patients and methods

This was a prospective, single-center study. Infants' enrolment in the study was carried out by physicians from the neonatal unit. The physician's role was to explain to the infant's parents or legal representatives the aims, procedures, advantages and disadvantages, benefits and risks involved in participating in the study. He also had to obtain the parents or legal representatives' written informed consent. The study was approved by the ethic committee: "*Comité de protection des personnes Sud Méditerranée*".

Criteria for inclusion in the study were: preterm infants less than 28 weeks of amenorrhea (WA) born in the "*Hôpital Nord*" in Marseille between January 2008 and January 2009, gestational age known with certainty, absence of genetic diseases, progressive neurological diseases, or malformations, and infants whose parents or legal representatives had consented to the infant participating in this study and signed the written informed consent form.

Non-inclusion criteria were: infants born strictly >28 WA, infants with a genetic disease, progressive neurological disease, or malformations, infants whose parents or legal representatives did not consent to the infant participating in the study, and infants born in another hospital or whose follow-up was scheduled to take place in a center that was closer to the parents' home.

Exclusion criteria were: deceased infants, infants whose parents withdrew their consent before the end of the study, infants who were not videotaped at least once before term age (during the WM period), and infants who were not videotaped during the FM period.

The antenatal, perinatal, and postnatal data were collected prospectively from the computer database of the neonatal unit. The quality of the data entered into the database was checked twice by two physicians using the medical file of each infant and "Qlick view" data management software.

2.1. Analysis of spontaneous motor activity

Two moments of video recordings were planned: the first between 30 and 40 weeks of age, and the second during the third month. The responsible brain structure of WMs, is the central generator pattern, it is a subcortical aréa. The emergence of the FMs coincides with the appearance of neurons with synaptic vesicles in the cortical subplate. [17].

The first time of recording was made in the hospital during the initial hospitalization of the infant, which is the WM period. Three recordings were required in order not to overestimate abnormal movements, especially poor repertoire movements (PR) [10]. A second time of recording was made during the FM period (i.e., between 9 and 20 weeks post-term). If there was still any doubt regarding the quality of these movements (abnormal or absent), the infant was reassessed 2 weeks later.

At the time of the recordings, the infant had to be calm and awake, and could not be crying or eating. The premature infants were filmed for 30–60 min, naked, in the incubator. Term infants were filmed for 5–10 min, wearing few clothes but in a room where the temperature was comfortable. An observer had to be present but not visible in order to ensure the infant's safety as well as compliance with the aforementioned conditions.

These recordings were reviewed by two different investigators who were trained in Prechtl's method. Qualitative and semi-quantitative assessments of the quality of the GMs were performed [15].

WMs were classified qualitatively as normal, cramped synchronized, hypokinetic, poor repertoire, or chaotic movements. The parameters studied in a semi-quantitative fashion were the movements' fluidity and amplitude, spatiotemporal variability, and speed, which were rated on a scale of 8–16.

Overall trajectory of WMs was defined as normal if movements were normal during all recordings, and the overall trajectory of WMs was defined as transitory abnormal if there was one anomaly in at least one of the recordings.

FMs were classified in a qualitative fashion as normal, absent, or abnormal.

Abnormal trajectory of GMs was defined as the infant having an abnormal or transitory abnormal motor activity at the WM age with absent FMs.

During the FM recording, the spontaneous movement quality was analyzed in a semi-quantitative fashion. The parameters studied were posture, fluidity of movements, quality of concurrent movements, and adequacy of the motor repertoire for the infant's age [14]. A normal posture was defined as the disappearance of the asymmetrical tonic neck reflex, the head being on the median line, and ability to move the fingers independently. Normal concurrent movements were the infant kicking his feet, grabbing his clothes, and playing with his hands. An adequate repertoire for the infant's age was defined as having sufficient concurrent movements, correct posture, and antigravity movements at the age of 3–5 months. Each parameter was assessed semi-quantitatively and given a note: 1, 2, or 4.The overall score ranged from 5 to 20.

2.2. Electroencephalography

Conventional EEG recordings were made using eight channels (Fp2, C4, T4, O2, Fp1, C3, T3, O1) and six leads (FP1-C3, C3-O1, O1-T3 and FP2-C4, C4-O2, O2-T4), mounted according to the 10–20 system (10 μv/mn and 15 mm/s). The recordings lasted 45–60 min in order to document the various stages of sleep. A simultaneous recording of the respiratory rate was obtained, and an ECG was recorded. All recordings were made according to the national protocol [18].

EEGs were analyzed by the same investigator, who was blind to the clinical findings and potential concomitant diseases. Analysis of the recordings was based on the evaluation of quantitative aspects and wave forms of normal and pathological EEGs in premature infants [18]. When several anomalies were associated, the presence of abnormal graphoelements (such as rolandic spikes or electrical seizures) was noted without taking into account the background EEG abnormalities. The criteria of Clancy and Tharp were used to assess background activity [19,20].

Abnormal EEG trajectory was defined by one or two abnormal EEG at 36 WA, and a transitory abnormal trajectory by at least one EEG abnormal and a normal EEG at 36 WA.

2.3. Brain ultrasonography (US)

US was performed in infants weighing <1 kg at day 3 (D3)/D5, D10/D14, D28, and upon hospital discharge. For infants weighing ⩾1–1.2 kg, US was performed at D3/D5, D10/D14, and upon hospital discharge.

Specific lesions were classified into type I–IV intraventricular hemorrhages (IVH) according to Papille [1] and leucomalacia LPV [21]. US lesions were regrouped into two severity grades: grade I with normal US or mild abnormalities (normal, IVH I, and IVH II), and grade II with severe abnormalities (IVH III and IVH IV).

2.4. Brain MRI

The assessment was carried out without sedation (after a bottle feeding) between 36 and 41 WA using conventional T1 and T2-weighed sequences, a T2 gradient echo sequence, and a diffusion sequence ($b = 0$, 500, 1000).

Lesions in preterm infants were classified by Paneth according to their anatomical distribution [21–23]. In our study, the modified Paneth classification, comprised of six different MRI types, was used: (1) normal MRI; (2) localized white matter abnormality; (3) subependymal and intraventricular non-parenchymatous hemorrhage; (4) myelinization delay; (5) diffuse white matter abnormality; (6) other lesions in the central grey nuclei or cerebellum. MRIs were classified into two severity grades: Grade I was comprised of normal MRIs and mild abnormalities (types 1–4) while grade II included severe abnormalities (types 5 and 6).

2.5. Neurological follow-up

Infants were called-in at the term age, at 3 months corrected age, every 3 months during the first year, and every 6 months during the second year. Neurological assessment was performed according to Amiel–Tison, and the assessment of psychomotor development was based on the Denver scale [24]. The clinical assessment was aimed at detecting minor motor abnormalities, a potential developmental delay, or established motor abnormalities (suspicion of cerebral palsy) (Fig. 1 and Table 4).

2.6. Study population (Fig. 1)

In total, 54 infants were born at 23–28 WA in the *Hôpital Nord* of Marseille between January 2008 and January 2009. Of these, 29 patients died during the neonatal period (75% stillbirths, 10.7% fetal deaths in utero, and 14.2% care limitations), and five other patients could not be included because the parents' home was too far away. Twenty infants total were included in the study. However, one patient died after 28 days and therefore was not included in the analysis.

Among the 19 patients included in the analysis, the mean age was 26.52 WA (range 25–27 $\pm$ 0.6), and the mean weight was 957 g (range 610–1200 $\pm$ 200). Of these, 36.8% (7/19 cases) had chronic lung disease (CLD), 42.2% (8/19 cases) had nosocomial infections, 10.5% (2/19 cases) had grade II US, and 33.3% (8/19 cases) had grade II MRI.

Patients were followed up until they reached the actual age of 14 months on average (range 8–20 $\pm$ 4.5).

The antenatal, perinatal, and postnatal characteristics of the study population are summarized in Table 1.

2.7. Statistical analyses

First, a descriptive analysis of the main social, demographical, and clinical characteristics was performed on the entire study population. Qualitative variables were presented as percentages, while quantitative variables were shown as means with standard deviations or medians with minimum and maximum values. The influence of perinatal and postnatal factors and spontaneous motor activity were analyzed using Pearson's chi-squared test. For theoretical effects <5, Fisher's exact test was used. For quantitative variables, non-parametric tests were used which considered the sample size and

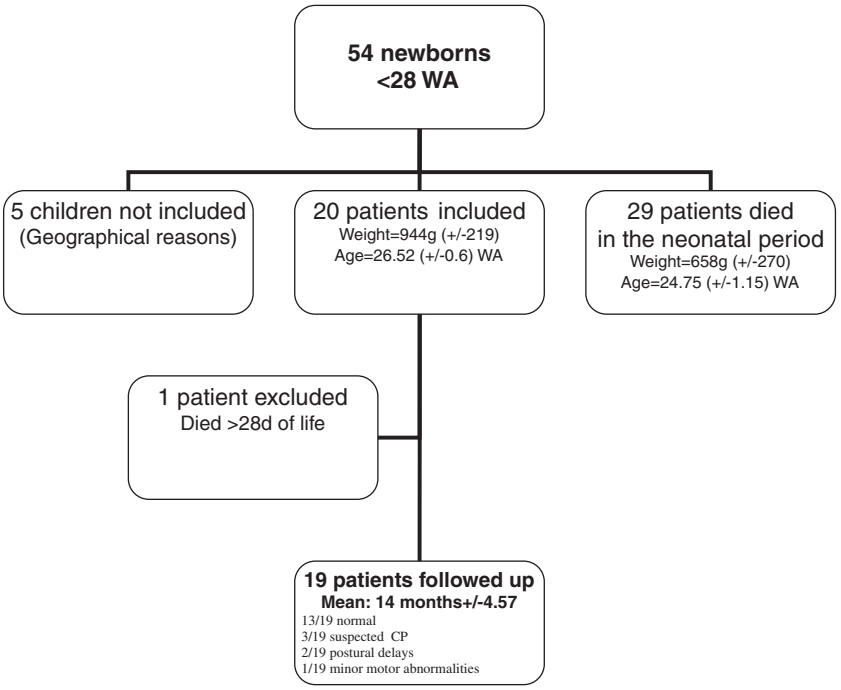

Fig. 1.

Table 1
Antenatal, perinatal, and postnatal data.

Antenatal, perinatal, and postnatal data	Number (*n*)	(%)
Prematurity etiologies		
"Infectious" context (chorioamnionitis, PROM, preterm labor)	15/19	79.5
"Vascular" context (PIH/PE/HELLPS)	4/19	21.2
IUGR	3/19	15.8
Antenatal corticotherapy	18/19	94.7
Cesarean delivery	10/19	52.6
Sex-ratio (male/female)	14/19	78.9
GA at birth in WA (median)	19/19	26
Mean BW in grams (±SD)	19/19	957 (±200)
Mean Apgar score at 5 min	19/19	7.26 (±2.6)
Chronic lung disease (CLD)	7/19	36.8
Apnea syndrome	15/19	79.5
Necrotizing enterocolitis (NEC) (all stages)	6/19	31.6
Materno-fetal infections	1/19	5.3
Nosocomial infections	8/19	42.2
Blood transfusions	17/19	89.5
Mean number of units per patient (±SD)	17/17	1.79 (±1.1)
Patent ductus arteriosus	9/19	44.4
Abnormal brain ultrasonography	8/19	42.1
IVH I and II (grade I)	5/19	26.5
IVH III and IV (grade II)	2/19	10.5
Abnormal EEG	3/19	15.8
Cerebral MRI	18/19	94.7
Grade I	12/18	66.6
Grade II	6/18	33/3

SD: standard deviation; PROM: premature rupture of membranes; PIH: pregnancy-induced hypertension; PE: pre-eclampsia; HELLPS: hemolysis, elevated liver enzymes, low platelet syndrome; IUGR: intrauterine growth retardation; GA: gestational age; WA: weeks of amenorrhea; BW: birth weight; CLD: chronic lung disease; NEC: necrotizing enterocolitis; PDA: patent ductus arteriosus; IVH: intraventricular hemorrhage; EEG: electroencephalogram; MRI: magnetic resonance imaging.

the distribution of the variables: the Mann–Whitney test when comparing two groups or the Kruskal–Wallis test when there were more than two groups to compare.

The specificity and the sensibility of the SMQ was calculated for predictive the abnormal neurological outcome for a cut off <15.

3. Results

3.1. Spontaneous motor activity

The GM characteristics assessed on the 73 video recordings are summarized in Tables 2 and 3. In 26.3% (5/19) of the cases, the infants showed normal WMs in all of the recordings (or normal trajectories). An abnormal trajectory was noted in 42.1% (8/19) of cases, while 31.5% (6/19) of cases showed a transitory abnormal trajectory.

Among the 55 WM recordings, one infant had chaotic movements, and none had hypokinetic movements.

During FM period, recorded at 52.4 WA on average (range 47–5 ± 2.7), FMs were normal in 78.9% (15/19), absent in 15.9% (3/19), and abnormal in 5.3% (1/19) of cases.

The overall mean score of the spontaneous movement quality at 3 months corrected age was 15.95/20 (range 5–20 ± 4.4). The motor repertoire was adequate for the infant's age in 78.9% (15/19), fluidity was optimal in 78.9% (15/19), concurrent movement quality was optimal in 63.2% (12/19), and 31.6% (6/19) of the cases showed an optimal posture.

In the WM recordings, an abnormal trajectory was noted in eight of the 19 infants (42.1%), with a normal trajectory observed in 11 infants (57.9%). In infants with an abnormal WM trajectory, the spontaneous movement quality score was 15.23 (CI [11.11; 19.39]) versus 16.45 (CI [13.68; 19.23]) in infants with a normal WM trajectory; the difference between the two groups was not statistically significant ($p = 0.397$).

3.2. Correlations between GMs and antenatal factors

There was no significant correlation between antenatal factors and GMs.

3.3. Correlation between GMs and perinatal factors

The abnormal GM trajectory (4/19 cases) correlated with gestational age ($p = 0.023$), as 50% of the infants with a gestational age ⩽26 WA presented an overall abnormal trajectory. Likewise, the spontaneous movement quality score at 3 months corrected age was also related to gestational age, as the infants with a gestational age ⩽26 WA (8/19 cases) had a mean score of 13.78 (CI [9.86; 17.69]) versus 17.90 (CI [16.04; 19.76]) for infants with a gestational age >26 WA (11/19 cases) ($p = 0.036$).

Lastly, the absence of FMs correlated with gestational age ($p = 0.033$), as 100% of infants >26 WA (10/19 cases) showed FMs, while 33% of infants ⩽26 WA (3/19 cases) showed no FMs.

No correlation between birth weight and hypotrophy was found.

3.4. Correlation between GMs and postnatal factors

Eight children had confirmed nosocomial infections, which correlated with the recorded WM quality at one recording: 87.5% (7/8 cases) of the infants with confirmed nosocomial infections had abnormal or transitory abnormal GM trajectories ($p = 0.05$). The longer of the duration of the parenteral nutrition, the more the quality of the WMs was altered ($p = 0.012$; Spearman coefficient −0.578). The number of central catheter was inversely correlated with the WM quality ($p = 0.034$; Spearman coefficient −0.503).

A correlation was observed between the patent ductus arteriosus (PDA) and the quality of spontaneous

Table 2
Quantitative and qualitative analysis of GMs.

N/GA	GA WM 1	WM 1	Score/16 WM 1	GA WM 2	WM 2	Score/16 WM 2	GA WM 3	WM 3	Score/16 WM 3	Traj. G. WM	FM	Score G. 3 months /20	GA FM	Motor rep.	Mvt smooth ness	Competing mvts quality	Posture
n 1/27	35	PR	13	36	PR	12	37	PR	12	ABN	N	15	52	4	2	4	1
n 2/26	36	CS	11	38	PR	10	39	CS	9	ABN	Absent	11	56	2	4	2	2
n 3/27	33	PR	10	40	PR	8	42	PR	9	ABN	Absent	5	52	2	2	1	1
n 4/27	31	PR	10	32	N	16	33	PR	9	TABN	N	20	50	4	4	4	4
n 5/27	31	N	16	34	PR	13	36	N	16	TABN	N	20	56	4	4	4	4
n 6/26	34	N	16	35	N	16	37	N	16	N	N	18	47	4	4	4	2
n 7/26	35	PR	11	35	PR	11	42	PR	17	ABN	N	17	56	4	4	4	1
n 8/27	32	Ch	12	33	N	16	34	N	16	TABN	N	20	50	4	4	4	4
n 9/26	35	N	16	36	N	16	37	N	16	N	Absent	8	52	2	2	1	2
n 10/25	31	PR	13	37	PR	13	40	PR	14	ABN	N	20	50	4	4	4	4
n 11/27	30	N	16	36	PR	12	42	N	16	TABN	N	18	50	4	4	4	2
n 12/27	32	N	16	33	N	16	34	PR	12	TABN	N	12	52	2	4	1	1
n 13/27	35	N	16	35	N	16	40	N	16	N	N	20	52	4	4	4	4
n 14/26	35	PR	11		NR			NR		ABN	N	18	54	4	4	4	2
n 15/27	34	PR	11	35	PR	12	38	PR	12	ABN	N	18	50	4	4	4	2
n 16/26	32	N	16	32	N	16	35	N	16	N	ABN	12	52	4	2	2	2
n 17/26	35	N	16	36	PR	13	40	PR	14	TABN	N	15	56	4	4	1	2
n 18/27	34	PR	10	36	PR	11	44	PR	11	ABN	N	18	52	4	4	4	2
n 19/27	32	N	16	35	N	16	40	N	16	N	N	18	57	4	4	2	4

N/GA: patient number and gestational age; GA WM 1: gestational age at 1st WM recording; WM 1: 1st WM recording; Score/16 WM 1: quantitative WM assessment at 1st recording, with a maximum of 16 (the same for WM 2 and 3); Traj. G. WM: trajectory of WM recordings; Score G. 3 months/20: semi-quantitative FM assessment, with a maximum of 20 performed at 3 months of corrected age; GA FM: age at FM recording; Motor rep.: analysis of motor repertoire at 3 months corrected age; mvt: movement.
N: normal; ABN: abnormal; TABN: transiently abnormal; PR: poor repertoire; Ch: chaotic; CS: cramped-synchronized; 18 optimal score WM; 20 optimal score QMV FM; NR: not interpretable (cries).

Table 3
Analysis of spontaneous motor activity (WM and FM).

Writhing movement	Recording 1 Mean GA 33.26		Recording 2 Mean GA 35.22		Recording 3 Mean GA 38.33	
Normal	8/19	42.4%	8/19	42.4%	8/19	42.4%
Poor repertoire	9/19	47.7%	10/19	53%	9/19	47.7%
Chaotic	1/19	5.3%	0/19	0%	0/19	0%
Cramped synchronized	1/19	5.3%	0/19	0%	1/19	5.3%
Global score (mean ± SD)	13.47	(±2.5)	13.5	(±2.5)	13.72	(±2.8)
Motor activity at 3 months corrected age mean GA 52.42			Number (%)			
Fidgety movement						
Normal			15/19		78.9%	
Abnormal			1/19		5.3%	
Absent			3/19		15.9%	
Quality of competing movements						
4			12/19		63.2%	
2			3/19		15.8%	
1			4/19		21.1%	
Movement smoothness						
4			15/19		78.9%	
2			4/19		21.1%	
1			0/19		0%	
Appropriate motor repertoirelage						
4			15/19		78.9%	
2			4/19		21.1%	
1			0/19		0%	
Posture						
4			6/19		31.6%	
2			9/19		47.4%	
1			4/19		21.1%	
Global score (mean ± SD)			15.95		(±4.4)	

WMs ($p = 0.050$); 87.5% (7/8) of the infants with a PDA exhibited altered WMs.

The number of days during which invasive ventilation was applied was inversely related to the overall spontaneous movement quality score at 3 months ($p = 0.031$; Spearman coefficient −0.496). Similarly, a correlation between CLD and WM quality ($p = 0.034$) was observed; 85.7% (6/7) of infants with CLD showed abnormal WMs.

3.5. Correlation between GMs and EEG, MRI, and US (Table 4)

There was a correlation between the global trajectory of the GMs and an abnormal EEG ($p = 0.046$), as 100% of the infants with an abnormal EEG (3/19 cases) displayed an abnormal global trajectory.

EEG trajectories correlated with motor repertoire at 3 months corrected age ($p = 0.001$), as 100% of the infants with an abnormal EEG (3/19 cases) had a repertoire score $\leqslant 2$. It also correlated with the quality of concurrent movements, as 100% of the infants with an abnormal EEG (3/19) exhibited a concurrent movement quality score $\leqslant 2$ ($p = 0.038$).

Grade II US and posture observed at 3 months corrected age ($p = 0.035$) were correlated, as 100% of the infants with a grade II US (2/19 cases) showed a strongly pathological posture with a posture score of 1.

There was a correlation between MRI and FMs ($p = 0.039$), as 66% of the infants with no FMs (2/19 cases) exhibited an abnormal MRI.

There was no correlation between spontaneous movement quality (SMQ) score and MRI grade ($p > 0.05$).

Grade II MRI and posture observed at 3 months corrected age were correlated ($p = 0.005$), as 100% of the infants with a grade II MRI (6/19) had a posture score $\leqslant 2$.

3.6. Correlations between spontaneous motor activity and neurological assessments

The neurological assessments and the global trajectory of GMs were correlated ($p = 0.007$), as 100% of the infants with suspected cerebral palsy (3/19) presented an abnormal or transitory abnormal GM global trajectory. The mean SMQ score was significantly higher in normal infants than in abnormal infants [17.38 ± 2.95 versus 12.83 ± 5.6] ($p = 0.031$).

Table 4
Individual trajectory of GMs, outcome, and neurological abnormalities.

n	G	EEG trajectory	Global trajectory	Global score	US	TFE grade	MRI grade	Posture	Outcome
n 1	F	N	TABN	15	N	1	2	1	N
n 2	M	ABN	ABN	11	N	1	1	2	m. A.
n 3	M	ABN	ABN	5	IVH 4	2	2	1	d. A.
n 4	M	N	TABN	20	IVH 2	1	1	4	N
n 5	M	N	TABN	20	N	1	1	4	N
n 6	M	N	N	18	N	1	1	2	N
n 7	M	N	TABN	17	IVH 4	2	2	1	d. A.
n 8	M	N	TABN	20	IVH 2	1	NR	4	N
n 9	F	ABN	ABN	8	N	1	1	2	d. A.
n 10	F	N	TABN	20	IVH 1	1	1	4	N
n 11	F	N	TABN	18	N	1	1	2	N
n 12	M	TABN	TABN	12	IVH 1	1	2	1	N
n 13	M	TABN	N	20	N	1	1	4	N
n 14	M	N	TABN	18	IVH 1	1	2	2	N
n 15	M	N	TABN	18	IVH 2	1	1	2	N
n 16	M	N	ABN	12	N	1	1	2	N
n 17	M	N	TABN	15	IVH 1	1	1	2	N
n 18	M	N	TABN	18	N	1	2	2	PMR
n 19	F	N	N	18	N	1	1	4	PMR

n: patient number; G: gender; M: male; F: female; N: normal; ABN: abnormal; TABN: transiently abnormal; global trajectory: Wm + Fm; global score: score obtained at 3 months corrected age; outcome: clinical examination at 6 months ± 12 months;US: ultrasound brain; IVH: intraventricular hemorraghe; NR: technical failure; m. A.: minor motor abnormalities; d. A.: definitive abnormalities evoking CP; PMR: psychomotor retardation.

3.7. Specificity, sensibility, predictive positive value and predictive negative value of SMQ

The prevalence of abnormal neurological assessment was 15.8% in our population. The specificity of the SMQ was 93%, sensibility was 60%, positive predictive value (PPV) was 75% and, negative predictive value (NPV) was 86% to detect abnormal neurological outcome.

PPV was 75% and, NPV 93% to detect CP.

4. Discussion

To date, only a few studies have investigated the quality and the predictive value of GMs and the quality of the spontaneous movement at 3 months corrected age (SMQ) in extremely preterm infants [8,13,15]. Indeed, these extremely preterm infants are subject to physiological instability during intrauterine and neonatal life that may influence neurological functioning temporarily or permanently. Prechtl's method, which measures the functioning of the brain by assessing movements' quality, reveals more abnormal transitory or permanent movements, especially in very preterm infants [9,13].

Our study is very similar to published studies on extremely preterm infants, revealing an abnormal motor activity during the WM period in 60% of cases, with mean scores of 13 (optimal value = 16), of which 40% are poor repertoire movements [9,13]. In a similar study focused on the first 15 days of life, Bos et al. observed a higher number of abnormal trajectories (16/19 cases), mostly with poor repertoire, in 19 extremely preterm infants (<28 WA).

Since these infants run the highest risk developing neurological deficit, it is important to know what perinatal or postnatal factors relate to brain dysfunction.

A study conducted by Bos et al. has shown that WM quality may be altered during the acute phase of systemic infections [25]. A similar study has demonstrated that children who had undergone postnatal corticotherapy for CLD exhibit transitory alterations in their motor activity [26]. Therefore, major alterations of the GMs during the WM period may not necessarily be indicative of brain lesions, but may rather reflect the impact of exogenous factors. In line with Bos et al., in our study, we found a correlation between the WM during preterm recordings and the occurrence of nosocomial infections, CLD, and patent ductus arteriosus. At the FM period, such a correlation was no longer found. The absence of correlation with NEC is probably because our study is powerless (only 6 patients had NEC).

In our study, during the FM period, 21% (4/19) of infants presented an overall abnormal GM trajectory. These results correspond to abnormalities of GMs found in high-risk populations [9]. Overall, the abnormal GM trajectory and the SMQ do not seem to be related to perinatal factors, except for gestational age, which is an independent risk factor for minor or major sequelae at school age [2,24]. The lack of correlation between the WMs and SMQ observed in our study further emphasizes the physiopathological difference of these movements [8,9]. The responsible brain structure of Wms, is the central generator pattern, it is a subcortical area. The emergence of the FMs coincides with the appearance of neurons with synaptic vesicles in the cor-

tical subplate. The subplate is a transient structure wich lies between the periventricular white matter and the developing cortical plate. The subplate is the earlier maturing cortical structure. The hypothesis presupposes that the subplate has descending projections wich may directly or indirectly transmit information to the central generator pattern network in the brainstem and spinal cord. This transient cortical structure plays a pivotal role in the generation of the GMs complexity and variation. What explains their clinical difference between WMs and FMs but probably also their difference of predictive value [17].

4.1. GMs and neuroradiological assessments

Contrarily to the published results by Bos et al. [25], we did not find any correlation between normal WM trajectory and normal US. In other published studies, WM quality strongly correlated with periventricular hyperechogenicities [27]. In our own study, grade II US tended to be related to a lower SMQ, though the difference did not reach statistical significance. However, there was a strong correlation between posture and grade II US, which has not yet been reported in the literature.

Early MRI, performed at term [21], may reveal local or diffuse white matter abnormalities, intraventricular hemorrhages, myelinization delays, brain atrophies, and other lesions (central grey nuclei and cerebellum). MRI seems to be the best technique to explore the newborn brain, providing the opportunity to perform a complete anatomical evaluation and monitor the progression of the lesions as well as brain maturation. A normal examination is associated with an absence of motor sequelae in over 90% of cases. However, due to its technical constraints, such as the need for the patient to remain immobile, the duration of the procedure, and the necessity to transfer the patient to another locale, MRI is secondary to US [21,23,28,29].

We have observed a correlation between grade II MRI and overall abnormal trajectory [21]. A recent study involving 86 premature infants <30 WA has revealed a strong correlation between the infants' spontaneous motor activity at 1 month and 3 months corrected age and the presence of white matter abnormalities at MRI [30].

Lastly, we have found a correlation between the adequate motor repertoire at 3 months corrected age, the quality of concurrent movements during the FM period, and an abnormal EEG. Precht'l et al. [9,13] have shown that the EEG has a positive predictive value for the neurological outcome. Furthermore, Brévaut et al. [24] have underlined the strong correlation between background rhythm abnormalities and the occurrence of cognitive sequelae. A recent publication has also shown that concurrent movement abnormalities at 3 months are strongly correlated with attention disorders [14].

4.2. GMs and outcome

Most studies dealing with predictive validity of GMs of the neuro-developmental outcome at 12–24 months have shown that the sensitivity and specificity of GMs increase after birth; they exhibit the highest predictive value between 8 and 20 weeks post-term [9,13]. Our study confirms this correlation, especially during the FM period, with the analysis of the SMQ. However, in our extremely preterm population, WMs seem to reflect a transitory neurological alteration secondary to a morbid event rather than being predictive of the neurological outcome at 12–24 months [13,25]. Moreover, our study shows no correlation between WMs and FMs or SMQ.

In a study involving preterm infants <35 WA, Garcia has shown that the PPV(60%), NPV (80%) were lower as compared to populations at a lesser risk [8,13]. The author suggests the high number of false positives could be to the fact a large number of infants had a short follow-up and that they thus not able to identify infants with subtle neurological dysfunctions that could manifest in more severe problems later in life.

The assessment of SMQ appears to provide a better prediction regarding the long-term outcome of infants, thereby reducing the number of false positives in GM analysis performed between 8 and 20 WA. Indeed, a recent study of 65 infants <33 WA has shown a correlation between the SMQ and the neurocognitive outcome at 5 years of age. For example, FMs correlated with cerebral palsy, posture abnormalities correlated with IQ, and concurrent movement abnormalities correlated with attention disorders [14].

Our study is the first study to analyze SMQ in extremely preterm infants. Within this population, the rate of neurological morbidity at school age has been shown to be unusually high, with over 55% of extremely preterm infants having neurological disorders at school age, of which approximately 20% have severe disabilities (cerebral palsy or major comprehensive retardation) [2,24].

In our study population, the mean global movement quality score was 15.95, two-thirds of the children had an abnormal posture with a score $\leqslant 2$, and abnormal concurrent movements or inadequate movements for the infants' age were observed in 30% of cases. This is in line with what has been reported by Butcher et al. for infants <33 WA [14]. These results are in line with the neurological disorders at school age. It should be noted that our current follow-up is insufficient to permit interpretation of these figures.

Indeed the PPV and the NPV of SMQ in our study is powerful to detect neurological troubles than Garcia study.

However, FMs were absent in 15.9% of our cases, which is similar to the rate of cerebral palsy observed in infants <28 WA [2,13]. The SMQ still a valuable means to detect neurological disorders in our study.

4.3. Study limitations

This is a prospective, single-center study. One limitation of the study is its small sample size. Our sample, nevertheless, was representative of the infants born in the "Hôpital Nord", because all of the infants were included in our follow-up, except those who were either deceased or could not be included because of geographical reasons. The duration of the follow-up is insufficient to allow us to draw definitive conclusions regarding the long term predictive validity of GMs and SMQ in extremely preterm infants. Two years seems to be insufficient for follow-up observation.This is the preliminary results of our study, and we are following all the children until 6 years old, for evaluation the relationship of minor neurological disorders or intellectual development.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.braindev.2010.10.023.

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