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Poor repertoire General Movements predict some aspects of development outcome at 2 years in very preterm infants

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ABSTRACT

Background: Observation of the quality of endogenously generated "General Movements" has been proved to be a reliable and sensitive tool in the assessment of fragile neonates. The absence of fidgety movements at 2–4 months post-term is highly predictive of Cerebral Palsy. On the contrary, the presence of a poor repertoire pattern during the writhing period is not reliable in predicting motor or neurobehavioral disorders at any stage of development.
Aim: To examine if the presence of a PR pattern at 1 month post-term was associated with lower neurodevelopmental quotients at 2 years.
Study design: General Movements evaluation at 1 and 3 months and the Griffiths Scales of Mental Development at 2 years were administered to a sample of very preterm infants. Infants were divided into two groups: poor repertoire pattern group and normal pattern group. Student's *t* Test and Chi squared test and ANOVA were used to compare neonatal variables and results between the two groups.
Subjects: 79 very preterm infants (birthweight ≤1500 g or gestational age ≤32 weeks), born January 2003 to December 2006 who had a follow-up at 2 years.
Outcome measure: Griffiths developmental quotient at 2 years.
Results: The Poor Repertoire group had lower Gestational Age, lower Birth Weight, lower Apgar scores at birth and lower Developmental Quotient at 2 years. Eye and Hand Coordination (subscale D) was the domain mostly responsible for such a difference. Quality of fidgety movements (normal or abnormal fidgety) at 3 months did not show any correlation with outcome measures at 2 years.
Conclusion: The presence of a PR pattern at 1 month post-term seems to predict lower neurodevelopmental scores at 2 years especially in the domain of eye and hand coordination. Longer follow-up is necessary in order to ascertain if such difference will continue to persist at older ages.

1. Background

It is well known that preterm neonates are at increased risk for impaired neurodevelopmental outcome [1].

Very preterm infants display a high rate of cerebral palsy, up to 15%, and about half of them show some degree of motor impairment [2,3]. Moreover, a higher incidence of ADHD, border-line IQ, socio-emotional problems, and reduced quality of life is found in the literature focusing on very preterm infant outcome [4–6]. Despite the current availability of sophisticated techniques to study the neonatal nervous system, such as EEG, cranial ultrasound, MRI, MR spectroscopy, and evoked potentials, an early prediction of neurodevelopmental outcome is still challenging in most of the very preterm infants.

Observation of the quality of endogenously generated "General Movements" (GMs) is a non invasive tool which has been proved to be reliable and sensitive in the assessment of fragile neonates [7]. GMs show age-specific characteristics: at 36–38 weeks post-menstrual age there is a first transition from fetal/preterm GMs, characterized by abundant variation, into writhing GMs. These are characterized by small to moderate amplitude and slow to moderate speed. Fast and large extensor movements, which are elliptical in form, may occasionally occur. Patterns of abnormal GMs during the writhing period are: Poor Repertoire (PR), monotonously sequenced successive movements which do not occur in the complex way seen in normal GMs; Cramped-Synchronized (CS), rigid movements without normal smooth and fluent appearance

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where the limbs and trunk contract and relax simultaneously; Chaotic, movements of all limbs of large amplitude that occur in a chaotic order without fluency nor smoothness [7,8].

A second transition occurs at about 6–9 weeks post-term when the writhing pattern is gradually replaced by fidgety pattern of GMs. They are small movements of moderate speed, and variable acceleration of neck, trunk, and limbs in all directions which are continuously present in the awake infant, except during focused attention [7,8]. Abnormalities of fidgety pattern can be classified as: Abnormal Fidgety (AF), similar to normal fidgety but with moderately or greatly exaggerated amplitude, speed and jerkiness and Absent Fidgety (F-); in the latter case other kind of movements can be present.

Standardized observation of GMs can predict neurological outcome, in particular the absence of fidgety and the presence of cramped synchronized GMs is associated with the development of CP [7,9]. Moreover, a poor quality of fidgety GMs has been reported to predict minor neurological dysfunction (MND) at school age [10,11] and poor manipulative abilities at puberty [12]. Earlier GMs, during the writhing period, are considered less reliable in predicting CP [7,8]. Whether they are able to predict MND or fine manipulative disability is still a matter of debate. According to Nakajima [13] the presence of a PR pattern is not related to the neurological outcome at 8–10 years and only the assessment of fidgety movements in those preterm infants with PR GMs trajectories can predict the outcome. Likewise, according to Groen [14], abnormal writhing GMs are not significantly related to the development of coordination problems and fine manipulative disability at 9–12 years.

However, more recently, the ability of writhing GMs to predict neurological outcome, at least in the short period, has been reappraised. Snider [15] found that quality of GMs at term was significantly related to some aspects of functional gross motor performance at 1 year of age. Kodric [16] found that writhing GMs had a significantly higher sensitivity than fidgety GMs in predicting Bailey Mental Developmental Score at 2.5 years, while this was not the case for the Psychomotor Developmental Scale. A PR pattern was also very frequent (up to 70% of movement sequences) in a sample of infants with Autism Spectrum Disorder whereas an absent or abnormal fidgety was present only in 50.7% of the cases [17].

The primary objective of this study was to examine if the presence of a PR pattern at 1 month post-term could influence neuromotor and neurobehavioral development at 2 years of age in a large group of very preterm infants. A secondary objective was to disclose which neurodevelopmental domain was more impaired.

2. Patients and methods

This study came from a longitudinal design to follow the neurological development of very preterm infants through 8 years of age. The study was approved by the ethical commission of Santa Croce and Carle Hospital, Cuneo, Italy.

Infants were enrolled from consecutive newborn admissions to the Neonatal Intensive Care Unit (NICU) of Santa Croce and Carle Hospital between January 2004 and December 2007. In that period 212 neonates with birth weight (BW) ≤1500 g or gestational age (GE) ≤32 weeks were admitted in NICU. Twenty of these died and 113 could not join the study group because of several reasons: denied permission to video-record the baby, returning to the town of provenance, moving to other geographical areas during follow-up period, absence at the scheduled follow-up visits. The remaining 79 infants (40 girls and 39 boys) formed the study group. They showed lower GE (p = ≤0.05), lower BW (p = 0.062) and no difference in gender prevalence and social characteristics, compared to the infants who were lost. Videotape recording and Griffiths test administration were part of the follow-up program and coincided with the scheduled clinical appointments. Informed consent was obtained from parents.

Videotape recording of GMs was obtained at 1 month post-term and 3 months post-term. The infants were videotaped for 15 min in outpatient clinics, lying supine, partially dressed, during period of active wakefulness. The quality of GMs was rated on the basis of the video recording by two assessors (El.B. and M.M.) who were blind to the medical history and perinatal course. All video-recordings were scored by each assessor independently. Inter-scorer agreement was 89%. If case discrepancies occurred, videos were reassessed and discussed until consensus was reached.

The findings in the writhing period were classified as normal (N), poor repertoire (PR) or cramped synchronized (CS). No chaotic movement was recorded. In the fidgety period they were classified as normal (N), abnormal (AF) or absent GMs (F-). On the basis of GMs pattern during the writhing period, neonates were divided in two groups: a PR group and a N group.

At 2 years, the Griffiths Scales of Mental Development (Griffiths Scales) [18] were carried out by E.B. who was masked to GMs results. The Griffiths Scales provide a general Developmental Quotient (DQ) in addition of five domains of functioning; each of them is assessed on a separate subscale: subscale A (Locomotor), subscale B (Personal/Social), subscale C (Hearing and Speech), subscale D (Eye and Hand Coordination) and subscale E (Performance).

As first step, Student's *t* Test was used to compare variables and results between the two groups. The Chi squared test was used to investigate differences concerning gender. As second step, an ANOVA was performed to control for the effect of GA, BW, Apgar score and gender. Differences with a *p*-value ≤0.05 were considered to be statistically significant.

3. Results

Three infants (2 males, 1 female) developed cerebral palsy during the follow-up. They showed CS movements at 1 month and F- at 3 months. Since our aim was to study the relationship between poor repertoire pattern and development at 2 years, these infants were excluded from the analysis.

Twenty neonates, out of the 76 left, showed a PR pattern while 56 had a N pattern of GMs at the corrected age of 1 month. As shown in Table 1, neonates with PR had lower Gestational Age (GA), lower birth weight (BW) and lower Apgar scores at 1 min. Although PR pattern was more frequent in males than in females, this difference was not significant (Table 1).

In Table 2 differences in ultrasounds (US) findings and neonatal morbidity are reported.

In Table 3 mean scores at Griffiths Scales at 2 years are shown. Group N infants obtained a significant higher Developmental Quotient (108 ± 10.7) than PR infants (97 ± 11.9). Such a difference was not significant in all the domains: Hearing and Speech (subscale C), Eye and Hand Coordination (subscale D) and Performance (subscale E) showed significant differences whereas Locomotor (subscale A) and Personal/Social (subscale B) did not.

Table 1
Influence of neonatal variables on writhing GMs (in bold when p = <0.05).

Neonatal variables	Normal writhing (56 infants)	Poor repertoire (20 infants)	p
	Mean ± s.d.	Mean ± s.d.	
Birthweight (g)	1241 ± 391	1017 ± 333	***0.025***
GA (weeks)	30 ± 2.26	28 ± 2.65	***0.002***
Apgar 1st minute	6 ± 2.13	4 ± 2.44	***0.000***
Apgar 5th minute	7 ± 1.09	6 ± 2.06	*0.267*
Male	27	13	
Female	29	7	*0.201*

Table 2
Ultrasound findings and neonatal morbidity (in bold when p = <0.05).

Neonatal morbidity	Normal writhing (56 infants)	Poor repertoire (20 infants)	p
US abnormalities	12	8	*.186*
RDS	43	13	*.464*
BPD	3	3	*.583*
Hyperbilirubinemia	45	10	***.021***
Sepsis	3	1	*.602*
NEC	2	4	*.063*
ROP	4	2	*.939*
PDA	14	7	*.514*
Hypoglycemia	19	4	*.379*
Hypocalcemia	7	5	*.338*
Severe anemia	7	5	*.338*

US abnormalities: IVH grade I or transient periventricular echodensities; RDS: respiratory distress syndrome; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; ROP: retino-ophthalmopathy of prematurity; PDA: patent ductus arteriosus.

Even after having excluded by ANOVA the influence of GA, BW, Apgar score and gender, the difference in DQ and subscale D (Eye and Hand Coordination) remained still significant.

At 3 months, only 4 infants showed abnormal fidgety (3 with previous PR and 1 with N writhing movements). They did not undergo any particular treatment and all of them had a normal DQ at 2 years. There was no significant difference between infants with AF and infants with NF as regards perinatal variables and outcome measures.

4. Discussion

Observation of the quality of GMs is widely used in the neurological assessment of fragile neonates. It is well known that the presence of CS pattern in the writhing period and an absent fidgety at three months post-term are highly predictive of CP [7]. Mildly abnormal fidgety movements are known indicators of minor neurological impairments, ADHD, and aggressive behavior at school age [10–12,14].

The prognostic value of PR pattern during the writhing period is less clear. Two studies failed to find any association with minor neurological impairments, coordination problems and fine manipulative disability at school age and at puberty [10,12]. However, two other studies reported that PR pattern was able to predict some aspects of development at 12 and 30 months [14,15].

In our small study we found that a poor GMs quality is related to lower developmental quotient at 2 years. Before discussing the clinical aspects of our study we wish to highlight some methodological limitations. First, we realize that our sample is a small one so extrapolation of our data to the general population is not correct. Second, Griffiths Scales are just a measure of neuro-behavioral development and they are not a diagnostic procedure. Third, someone could argue about excluding children with CP, however this should be considered a strength rather than a limitation as we were interested in the relationship between quality of GMs during the writhing period and later development in children without CP.

Table 3
Griffiths Scales of Mental Development outcome at 2 years. (ANOVA analysis included GE, BW, Apgar score and gender. In bold when p = <0.05).

Griffiths Scales	Normal writhing (56 infants) Mean ± s.d.	Poor repertoire (20 infants) Mean ± s.d.	p	p after ANOVA
Developmental Quotient	108 ± 10.7	97 ± 11.9		
Range	*75–123*	*68–112*	***.000***	***.003***
A (Locomotor)	116 ± 15.3	109 ± 13.8		
Range	*69–135*	*84–135*	*.076*	*.229*
B (Personal/Social)	112 ± 11.9	109 ± 11.6		
Range	*72–135*	*79–119*	*.333*	*0.891*
C (Hearing and speech)	99 ± 15.6	89 ± 20.3		
Range	*50–115*	*50–113*	***.026***	*.060*
D (Eye and hand coordination)	109 ± 11.3	97 ± 10.5		
Range	*81–123*	*81–112*	***.000***	***.000***
E (Performance)	110 ± 12.5	101 ± 18.7		
Range	*54–134*	*50–118*	***.019***	*.061*

Twenty preterm neonates of our sample (26%) showed a PR pattern at 1 month post-term. These infants had significant lower GA, lower BW and lower Apgar scores. This is not unexpected since risk for neurodevelopmental impairment increases as BW and GA decrease. As far as we know, the presence of a PR pattern denotes current mild dysfunction. However, in the post-natal period it is often followed by normal fidgety GMs, suggesting that it just reflects a temporary dysfunction [19]. Such an improvement occurred actually in 17 out of 20 of our infants of the PR group: only three of them showed an AF pattern at three months post-term.

Infants with PR pattern at 1 month had lower Griffiths Scale DQ at 2 years. Hearing and Speech (subscale C), Eye and Hand Coordination (subscale D) and Performance (subscale E) made a significant contribution to this result. After having removed the influence of GA, BW, and Apgar score at 1 min the difference was still significant for DQ and subscale D.

Two studies reported an association between quality of GMs in writhing period and development at 12 and 30 months. Snider and collaborators [14] reported that abnormal GMs at term were associated with worse motor performances at 1 year. In particular, Gross Motor Quotient at the Peabody Developmental Motor Scales and walking abilities at the Alberta Infant Motor Scales were significantly impaired. However, their results cannot be compared with ours since in their study infants with PR and CS movements were grouped together and we know that CS are highly predictive of CP and motor impairment [9]. Kodric [15] assessed GMs in 26 preterm infants at term age and followed them up to 2.6 years when the Bayley Scales of Infant Development was administered. Five out 26 of their infants showed a N pattern at term age, 15 showed a PR pattern and 6 showed a CS pattern. Infants with N pattern at term age obtained the highest scores on Mental Developmental Index, those with PR had lower, and those with CS had the lowest scores. The same trend was found for the results of the Psychomotor Developmental Index, but the differences were not significant. The authors stated that even excluding infants with CP, writhing GMs at term age have a high sensitivity in detecting children with mildly or significantly delayed performance on Bayley Mental Developmental Index at 2.6 years post term. The Bayley Mental scale evaluates several types of abilities: sensory/perceptual acuities, discriminations, and response; acquisition of object constancy; memory learning and problem solving; vocalization and beginning of verbal communication; basis of abstract thinking; habituation; mental mapping; complex language; and mathematical concept formation.

Our data go in the same direction: the presence of a PR pattern in very preterm infants is associated with a lower DQ at 2 years. In our sample, as well as in Kodric's one, locomotor domain was not impaired. Lower results in Hearing and Speech, Eye and Hand Coordination and Performance were linked to PR pattern at 1 month. According to our data one could hypothesize that neural networks generating writhing GMs were different from those generating fidgety GMs and that their non-optimal development could be linked to some impairment in neurodevelopmental domains different from locomotor one. However, no evidence is available suggesting that the basic neural network underlying writhing GMs differs from those of fidgety GMs [20]. It is possible that a better differentiation of fidgety GMs could have resulted in a similar relationship with developmental outcome at 2 years.

We do not know if such link will disappear or will still be present at school age. However, Largo and collaborators [21] showed that Griffiths scales at 2 years could reliably predict mental performance at school age for normal and learning disabled children. Prediction was less accurate for children with border-line performances (DQ between 70 and 90). In their study, Hearing and Speech (C), Eye and Hand Coordination (D) and Performance (E) were the best predictors of mental functioning also in the border-line group.

In conclusion, according to our findings, a PR pattern at 1 month seems to be actually associated with a worse neurobehavioral development at 2 years of age in a group of very preterm infants. Eye and Hand Coordination is the neurodevelopmental domain which appears to be the most impaired. More research in this field is needed to confirm our data and to discover if they can have a clinical meaning. In order to ascertain if the difference between the PR group and the N group will persist through childhood it is our intention to follow the same children up to 8 years of age and to produce a report every year.

Conflict of interest statement

The authors declare that they have no competing interests.

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