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Neonatal neurological examination during the first 6 h after birth☆



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ABSTRACT

Background: Few neurological assessments are easily performed during the first 6 h after birth.

Aims: To assess a cohort of low risk term born newborns within the first 6 h and at 48 h after birth using the Hammersmith Neonatal Neurological Examination.

Study design and subjects: A population of low risk term born newborns was examined within 3 h from birth or between 3 and 6 h. Each infant was re-assessed at 48 h, establishing the range and frequency distribution of neonatal neurological scores at each time point.

Results: Of the 124 full-term born newborns, 62 were assessed at 0–3 h and 62 at 3–6 h. All infants were reassessed at 48 h. For 23/34 of the neurological items, the range and median scores were similar across the 3 time points. In the remaining 11 items the three groups had a similar range of scores but the median scores were different with different rates of changes. In 6 of the 11 the median scores at 3–6 h were similar to those observed at 48 h but they appeared to be 'less mature' at 0–3 h. Only in one item the median scores were consistently different at the 3 time points.

Conclusions: Our results suggest that a neurological examination can already be reliably performed soon after birth. These findings will help in the interpretation of the few items that show changes with increasing postnatal age.

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1. Introduction

In the last 10 years the advent of therapeutic hypothermia as a neuroprotective intervention in newborns with hypoxic ischemic-encephalopathy (HIE) [1,2] has raised the issue of defining early clinical indicators of neurological status. Therapeutic hypothermia is used to cool infants with moderate or severe HIE within 6 h of birth to a body temperature between 33.5 °C and 34.5 °C and maintain this degree of cooling without interruption for 72 h [3]..

Because of the timing, early assessments are needed to define inclusion criteria. These generally include: i) a gestational age \geq 35 weeks, ii) a perinatal hypoxic ischemic event defined by low Apgar scores or fetal acidosis and an evidence of moderate or severe encephalopathy according to the Sarnat Score that identifies 3 different stages considering the

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alertness, global tone, some reflexes and the electroencephalogram (EEG) activity [4].

Although the Sarnat score is widely used in both clinical and medical research, it has been suggested that other early neurological tools may provide additional clinical information, especially in the intermediate clinical grading. While infants with Sarnat stage 1 tend to have a normal outcome, and those with stage 3 to develop neurological sequalae, infants with stage 2 have been found to be associated with both normal and abnormal outcome [2].

There is therefore the need to identify other neonatal neurological assessments that could be easily performed during the first 6 h after birth to provide more detailed information on the neurological status and on prognosis that may prove to be useful in infants with moderate asphyxia.

The Hammersmith Neonatal Neurological Examination (HNNE) developed by Dubowitz and Dubowitz, in 1981 and revised in 1999, is widely used in preterm and term born newborns, both in clinical and research settings [5]. This assessment has proved to be useful in identifying specific clinical patterns related to distinct neuroimaging findings and to predict prognosis [6–8]. This examination however has only

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been used after the first 6 h after birth and no normative data on earlier examination are available.

The aims of the present study were: a) to assess a cohort of low risk term born newborns within the first 6 h after birth and at 48 h using the HNNE and b) to establish the range and frequency distribution of neonatal neurological scores in this age range.

2. Methods

The newborns included in the present study were recruited from the Neonatal Unit of our Hospital from December 2014 to March 2016. Infants were consecutively enrolled if

- 1. they were born between 38.0 and 41.6 weeks' gestational age (GA);
- 2. their cranial ultrasound scans (US) were normal or showed only transient flares or germinal layer hemorrhages during the first postnatal week [6]; and
- 3. their clinical condition was stable during the first days after birth.

The US assessments were part of the protocol for the present study and were performed and interpreted by two experiences neonatologists (FG and FS).

We excluded infants with major congenital anomalies, genetic or chromosomal abnormalities, metabolic disorders, congenital or neonatal infection or any sign of encephalopathy or seizures during their neonatal course, jaundice requiring phototherapy or respiratory distress. Informed consent was obtained for all infants. The study protocol was previously approved by the Ethics Committee of our Institution.

2.1. Clinical examination

The HNNE, consisting of 34 items, grouped in six categories (tone, tone patterns, reflexes, movements, abnormal signs and behaviour), was performed and recorded using the standardised scoring sheet [5].

The infants were examined undressed on an open bed or in their cot in a warm quiet room. Behavioural state, graded according to Brazelton criteria [9] at the time of examination was recorded. In order to achieve comparable results, whenever possible, all the infants were tested in the same state, midway between feeds, predominantly in state 4 or 5 of sleep.

The scoring sheet consists of numbered columns, between 3 and 5 for each item. If an item falls between 2 columns, it is given the appropriate half score between the columns (e.g. items scoring between 2 and 3 scored 2.5; between 2 and 1 scored 1.5). These scores are defined as raw scores [5].

The infants were assessed within the first 6 h after birth.

The examinations were performed by one of the author (DMR) who was very familiar with the assessment and previously trained by the developers of the HNNE.

The results were analysed according to the time from birth into 3 subgroups: the first included the assessments within 3 h from birth and the second those between 3 and 6 h from birth. A third group included the assessments at 48 h from birth, that were performed in all the infants included in the first two subgroups.

The distribution of the raw scores (the column circled) was plotted for each item and the 10th centile taken as the cut-off point. It was then possible to compare the median and the 10th centile score for each item from the 3 subgroups.

All the infants included in this study had a similar level of care.

3. Results

A total of 124 full-term born newborns fulfilled the inclusion criteria (Table 1). Their GA was between 38 and 41 weeks. Sixty two of the 124 (30 female, 32 male) were assessed at 0–3 h and the other 62 (33 female, 29 male) at 3–6 h. All infants showed normal cranial US and were re-assessed at 48 h (range: 46–51 h).

Table 1 Characteristic of population.

| Gestational age (weeks) | 38.8 ± 1.0 |
|---|---------------|
| Gender (M/F) | 63/61 |
| Birth type (eutocic delivery/caesarean section) | 68/56 |
| Apgar score 1' | 8.9 ± 0.3 |
| Apgar score 5' | 9.9 ± 0.4 |

3.1. Range of scores and median score

3.1.1. Comparison between 0 and 3 h, 3-6 h and 48 h

3.1.1.1. Tone items. The median score was the same in 4 of the 10 items assessing tone in all the three assessments (i.e. within 3 h, between 3 and 6 h and at 48 h).

In 3 of the other 6 items (arm recoil, arm traction, leg traction), the median was the same in the assessments performed at 3 to 6 h and at 48 h while it was lower, expressing less "mature tone", in those examined within 3 h.

In the remaining 3 item (posture, head control 2, popliteal angle) the median was the same in the assessments performed within 3 h and at 3 to 6 h and higher, expressing more "mature tone, at 48 h.

The range of scores falling within the 90th centile at 48 h was different only in one item when compared to the findings at 3-6 h and in 5 items when compared to the findings at 0-3 h.

3.1.1.2. Tone patterns. The median score was the same in all the 5 items assessing tone patterns in all the three assessments.

The range of scores falling within the 90th centile at 48 h was different only in 2 item when compared to the findings at 3-6 h and in 2 items when compared to the findings at 0-3 h.

3.1.1.3. Reflexes. The median score was the same in 4 of the 6 items assessing reflexes in all the three assessments. In the remaining 2 items (palmar grasp and Moro) the median was the same at 3 to 6 h and at 48 h while it was lower, expressing immature responses, in those examined within 3 h.

The range of scores falling within the 90th centile at 48 h was different only in 1 item when compared to the findings at 3-6 h and in 4 items when compared to the findings at 0-3 h.

3.1.1.4. *Movements*. The median score was the same in all the 3 items assessing movements in all the three assessments.

The range of scores falling within the 90th centile at 48 h was different only in 2 item when compared to the findings at 3-6 h and in 3 items when compared to the findings at 0-3 h.

3.1.1.5. Abnormal signs. The median score was the same in 2 of the 3 items assessing abnormal signs in all the three assessments. In the remaining item (startles) the median was the same at 0 to 3 h and at 48 h while it was different at 3 to 6 h.

The range of scores falling within the 90th centile at $48\,h$ was different only in 2 item when compared to the findings at $3-6\,h$ and in 0 items when compared to the findings at $0-3\,h$.

3.1.1.6. Behavioural items. The median score was the same in 4 of the 7 items assessing abnormal signs in all the assessments.

In 1 of the other 3 (alertness) the median was the same in the assessments performed at 3 to 6 h and at 48 h and lower, expressing immature responses, in those examined within 3 h.

In the remaining 2 item (visual orientation, consolability) the median was the same at 0 to 3 h and at 3 to 6 h and higher, expressing more mature responses, at $48\ h.$

Table 2Median and range of scores of single items.

| | Median (10th-90th centile) | | |
|-------------------------------|----------------------------|---------|---------|
| | 0-3 h | 3-6 h | 48 h |
| Posture | 3 (3-3) | 3 (3-4) | 4 (3-4) |
| Arm recoil | 3 (2-4) | 4 (3-4) | 4 (3-4) |
| Arm traction | 3 (2-4) | 4 (3-4) | 4 (3-4) |
| Leg recoil | 4 (3-4) | 4 (3-4) | 4 (3-4) |
| Leg traction | 3 (2-4) | 4 (3-4) | 4 (3-4) |
| Popliteal angle | 3 (3-4) | 3 (3-4) | 4 (3-4) |
| Head control a | 3 (3-4) | 3 (3-4) | 3 (3-4) |
| Head control b | 3 (3-4) | 3 (3-4) | 4 (3-4) |
| Head lag | 3 (2-4) | 3 (3-4) | 3 (3-4) |
| Ventral suspension | 3 (2-4) | 3 (2-4) | 3 (3-4) |
| Flexor tone a | 3 (2-4) | 3 (2-3) | 3 (2-3) |
| Flexor tone b | 3 (3-3) | 3 (3-3) | 3 (3-3) |
| Leg extensor tone | 3 (2-3) | 3 (3-4) | 3 (2-4) |
| Neck extensor tone | 3 (3-3) | 3 (2-3) | 3 (2-3) |
| Increased extension tone | 3 (2-3) | 3 (2-3) | 3 (2-4) |
| Tendon reflex | 3 (3-4) | 3 (3-4) | 3 (3-4) |
| Suck/gag | 4 (3-4) | 4 (4-4) | 4 (4-4) |
| Plamar grasp | 3 (2-4) | 4 (3-4) | 4 (3-4) |
| Plantar grasp | 3 (3-3) | 3 (3-3) | 3 (3-3) |
| Placing | 3 (2-3) | 3 (2-3) | 3 (2-3) |
| Moro | 3 (2-4) | 4 (3-4) | 4 (3-4) |
| Spontaneous movement quantity | 3 (2-3) | 3 (2-4) | 3 (3-4) |
| Spontaneous movement quality | 3 (2-4) | 3 (2-3) | 3 (3-4) |
| Head raising | 3 (2-3) | 3 (2-4) | 3 (2-4) |
| Hand/toe posture | 2 (2-2) | 2 (2-3) | 2 (2-2) |
| Tremor | 2 (2-3) | 2 (2-4) | 2 (2-3) |
| Startle | 2 (1-3) | 1 (1-2) | 2 (1-3) |
| Eye appearance | 3 (1-3) | 3 (3-4) | 3 (3-3) |
| Auditory orientation | 2 (2-3) | 2 (2-3) | 2 (2-3) |
| Visual orientation | 2 (2-5) | 3 (2-5) | 4 (3-5) |
| Alertness | 2 (2-4) | 3 (2-4) | 3 (2-4) |
| Irritability | 2 (1-3) | 2 (1-3) | 2 (1-3) |
| Consolability | 2 (1-3) | 2 (1-3) | 3 (1-3) |
| Cry | 3 (1-3) | 3 (1-3) | 3 (1-3) |

The range of scores falling within the 90th centile at 48 h was different only in 2 item when compared to the findings at 3-6 h and in 1 item when compared to the findings at 0-3 h.

No differences on neurological scores (range and median) has been reported according to gender, GA or birth type.

Table 2 shows details of the median and range of scores of the single items.

4. Discussion

This is the first study assessing the neurological status of the newborn baby within the first 6 h after birth using the HNNE. This tool was originally validated in low risk term newborns assessed between 6 and 48 h, and has also been used in several research studies, always performed after the first 6 h [5–8,10,11]. As early intervention such as therapeutic hypothermia is becoming more and more available [1–3] and is planned within the first few hours after birth, there is an increasing interest in achieving more information on the neurological findings in the first hours after birth.

In this study we assessed a cohort of low risk term born newborns within the first 6 h after birth, with an equal number of assessments at 0–3 h and at 3–6 h. Our aim was to establish possible differences in the range and frequency distribution of early neonatal neurological scores between the two time points and to compare both with the scores obtained at 48 h, when all infants were re-examined.

The three groups of assessment had globally a similar range of scores and in most of the items (23 of the 34) (leg recoil, head control-A, head lag, ventral suspension, all the items of patter tone, tendon reflex, suck/gag, plantar grasp, placing, all the items assessing movements, abnormal hand or toe posture, tremor, eye appearance, auditory orientation, irritability and cry) the median were similar within the same column

or only one column of difference in all three groups (0–3, 3–6 and 48 h). Therefore for these items the interpretation of the findings used for older newborns could be used from birth.

In the other items the three groups also had a similar range of scores but the medians in the first hours after birth were different than those assessed at 48 h. The changes observed followed different trends. In 6 items (arm recoil, arm traction, leg traction, palmar grasp, Moro reflexes and alertness) the median obtained at 0–3 h appeared to be 'less mature' than those found at 3–6 h with the examinations performed at 3–6 h similar to those observed at 48 h. These items are probably more influenced by the delivery, needing of few hours to reach findings similar to that of 48 h.

In four items (posture, popliteal angle, head control B and consolability) the median were similar at 0–3 and 3–6 h but different at 48 h.

Only in the item on visual assessment the median was consistently different at 0–3, 3–6 and 48 h with the responses becoming more mature with increasing postnatal age. This is consistent with previous studies also showing a progressive improvement of visual function during the neonatal period especially for vertical and arc tracking due to a progressive exposition to light and extra uterine environment [12].

Our findings suggest that the neurological examination can already be reliably performed soon after birth as for most items there are no obvious differences of range or median of the findings compared to those observed after 6 h. Some caution should be used in the interpretation of the other items as 'less mature' responses such as those found in our cohort, should be interpreted as appropriate for age and not as abnormal signs. Rather than hypothesizing a maturation within few hours some items are likely to be affected by events occurring at the time of delivery and may require some time to adapt to extra-uterine life.

The number of newborns examined in this study was too small to allow a meaningful frequency distribution and obtain optimality scores for each subgroup as performed at the time of the validation of the HNNE [5]. It is of interest however that even in the items that had different medians at different ages, the findings falling outside the 90% were the same at both 0–6 h and 48 h, confirming that some neurologic signs are uncommon in healthy term born infants, regardless of the timing of the neurological assessment.

Finding these abnormal signs when examining newborns with brain lesions or HIE can further help, in combination with other tools such as cerebral function monitor, to identify the infants needing intervention.

Conflicts of interest

None.

References

- M.A. Rutherford, D. Azzopardi, A. Whitelaw, F. Cowan, S. Renowden, A.D. Edwards, M. Thoresen, Mild hypothermia and the distribution of cerebral lesions in neonates with hypoxic-ischemic encephalopathy, Pediatrics 116 (2005) 1001–1006.
- [2] A.J. Gunn, J.S. Wyatt, A. Whitelaw, J. Barks, D. Azzopardi, R. Ballard, A.D. Edwards, D.M. Ferriero, P.D. Gluckman, R.A. Polin, C.M. Robertson, M. Thoresen, CoolCap Study Group, Therapeutic hypothermia changes the prognostic value of clinical evaluation of neonatal encephalopathy, J. Pediatr. 152 (2008) 55–58, 58.e1.
- [3] R. Mosalli, Whole body cooling for infants with hypoxic-ischemic encephalopathy, J. Clin. Neonatol. 1 (2012) 101–106.
- [4] H.B. Sarnat, M.S. Sarnat, Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study, Arch. Neurol. 33 (1976) 696–705.
- [5] L. Dubowitz, V. Dubowitz, E. Mercuri, The Neurological Assessment of the Preterm and Full-term Newborn Infant, second ed. Mc Keith Press, 1999.
- [6] D. Ricci, Haataja L. RomeoDM, I.C. van Haastert, L. Cesarini, J. Maunu, et al., Neurological examination of preterm infants at term equivalent age, Early Hum. Dev. 84 (2008) 751–761.
- [7] E. Mercuri, D. Ricci, D.M. Romeo, Neurological and visual assessments in very and late low-risk preterm infants, Early Hum. Dev. 88 (Suppl. 1) (2012 Mar) S31–S33.
- [8] D.M. Romeo, D. Ricci, C. Brogna, S. Cilauro, RomeoMG LombardoME, et al., Neurological examination of late-preterm infants at term age, Eur. J. Paediatr. Neurol. 15 (2011) 353–360.

- [9] T.B. Brazelton, Neonatal Behavioural Assessment Scale. Clinics in Developmental
- [9] 1.8. Brazeloni, Neonatal Behaviolial Assessment Scale. Clinics in Developmental Medicine No. 50. London: Spastics International Medical Publications/ WilliamHeinemann Medical Books, JB Lippincott Co., Philadelphia, 1973.
 [10] A.J. Spittle, J.M. Walsh, C. Potter, E. Mcinnes, J.E. Olsen, K.J. Lee, P.J. Anderson, L.W. Doyle, J.L. Cheong, Neurobehaviour at term-equivalent age and neurodevelopmental outcomes at 2 years in infants born moderate-to-late preterm, Dev. Med. Child
- Neurol. (2016)http://dx.doi.org/10.1111/dmcn.13297.

 [11] A.J. Spittle, J. Walsh, J.E. Olsen, E. McInnes, A.L. Eeles, N.C. Brown, P.J. Anderson, L.W. Doyle, J.L. Cheong, Neurobehaviour and neurological development in the first month
- after birth for infants born between 32-42 weeks' gestation, Early Hum. Dev. 96 (2016) 7–14.
 [12] D. Ricci, D.M. Romeo, F. Serrao, L. Cesarini, F. Gallini, F. Cota, D. Leone, A.A. Zuppa, C.
- Romagnoli, F. Cowan, E. Mercuri, Application of a neonatal assessment of visual function in a population of low risk full-term newborn, Early Hum. Dev. 84 (2008)