Early Human Development 96 (2016) 7–14

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Neurobehaviour and neurological development in the first month after birth for infants born between 32–42 weeks' gestation

Alicia J. Spittle [a,b,c,*], Jennifer Walsh [b,d], Joy E. Olsen [b,c], Emma McInnes [b,c], Abbey L. Eeles [b,c], Nisha C. Brown [b,f], Peter J. Anderson [b,e], Lex W. Doyle [b,c,f], Jeanie L.Y. Cheong [b,c,f]

[a] Physiotherapy Department, University of Melbourne, 7th Floor Alan Gilbert Building, Grattan Street, Parkville, Victoria 3052, Australia
[b] Victorian Infant Brain Studies, Clinical Sciences, Murdoch Childrens Research Institute, The Royal Children's Hospital, Flemington Road, Parkville, Victoria 3052, Australia
[c] Newborn Research, The Royal Women's Hospital, 20 Flemington Rd, Parkville, Victoria 3052, Australia
[d] Pediatric Infant and Perinatal Emergency Retrival, The Royal Children's Hospital, Flemington Rd, Parkville, Victoria 3052, Australia
[e] Department of Paediatrics, University of Melbourne, The Royal Children's Hospital, Flemington Rd, Parkville, Victoria 3052, Australia
[f] Department of Obstetrics and Gynaecology, University of Melbourne, The Royal Women's Hospital, 20 Flemington Rd, Parkville, Victoria 3052, Australia

ARTICLE INFO

Article history:
Received 1 September 2015
Received in revised form 5 February 2016
Accepted 9 February 2016
Available online xxxx

Keywords:
Preterm infant
Newborn infant
Neurobehavioural assessment
Neurological examination

ABSTRACT

Aims: The objective of this study was to generate reference values for infants born moderate preterm (MPT), late preterm (LPT) and full term (FT) for three newborn neurobehavioural/neurological examinations in the first weeks after birth.

Study design: Prospective cohort study to examine the expected range of values for MPT (born 32^{+0} to 33^{+6}), LPT (34^{+0} to 36^{+6}) and FT (born 37 to 42 weeks' gestation) infants' performance on the Hammersmith Neonatal Neurological Examination (HNNE), the Neonatal Intensive Care Unit Network Neurobehavioural Scale (NNNS) and Prechtl's General Movements Assessment (GMA) in the first weeks after birth. Further, to determine the effects of sex, gestational age at birth, and postmenstrual age at assessment on the 3 different assessments within the gestational age groups.

Subjects: 80 MPT, 129 LPT and 201 FT infants were recruited shortly after birth from a tertiary hospital.

Results: The means, standard deviations and 5th, 10th, 25th, 50th, 75th, 90th and 95th centiles are presented for the HNNE and NNNS for each of the three gestational age groups. Overall, FT infants performed better than MPT and LPT infants. The rate of normal GMA within the first few weeks after birth was 25% for MPT, 32% for LPT, and 90% for FT infants. The effects of sex, gestational age at birth, and postmenstrual age at assessment varied between test and gestational age groups.

Conclusions: This study provides normative data for the HNNE, NNNS, and GMA administered within the first weeks after birth in a sample of MPT, LPT and healthy FT infants.

1. Introduction

In the first days and weeks after birth neonatal neurobehavioural and neurological assessments provide an insight into the integrity of the infant's central nervous system, which is important for identifying an infant's strengths and susceptibilities [1,2]. These assessments can be used to guide therapeutic interventions and identify infants requiring more intensive developmental surveillance [3]. Neurobehavioural assessments in the newborn period involve the assessment of a range of neurobehaviours such as an infant's ability to orientate to an inanimate object or how much they cry during an examination, whilst neurological assessments may involve items such as assessment of movement patterns, tone and reflexes [3–5]. Standardised neurobehavioural and neurological assessments administered within the first weeks after birth have been associated with long term cognitive, motor and behavioural outcomes [6–8]. There are a variety of neurobehavioural and neurological assessments for newborn infants with varying validity and reliability, and for differing purposes. Several reviews have recommended the NICU Network Neurobehavioural Scale (NNNS) [9], the Hammersmith Neonatal Neurological Examination (HNNE) [10], and the General Movements Assessment (GMA) [2] as useful tools for researchers and clinicians to identify infants at risk of long term adverse neurodevelopmental outcomes [1,4,11,12].

Neurobehavioural and neurological assessments can be safely completed within hours after birth if an infant is stable. Several studies have demonstrated neurobehaviour and neurological presentation changes within the first few weeks of life, including changes in muscle

Abbreviations: MPT, moderate preterm; LPT, late preterm; FT, full term; HNNE, Hammersmith Neonatal Neurological Examination; NNNS, Neonatal Intensive Care Unit Network Neurobehavioural Scale; GMA, General Movements Assessment.

* Corresponding author at: Physiotherapy Department, University of Melbourne, 7th Floor Alan Gilbert Building, Grattan Street, Parkville, Victoria 3052, Australia.
E-mail address: aspittle@unimelb.edu.au (A.J. Spittle).

http://dx.doi.org/10.1016/j.earlhumdev.2016.02.006
0378-3782/

tone, quality of movement, self-regulation and orientation [10,13–15]. Both the NNNS and HNNE provide cut-off scores to identify infants at risk of later neurodevelopmental impairment based upon the distribution of data from healthy term born infants [10,13]. This information is based upon data collected within the first few days after birth, whilst the infants are still in hospital. However, given that these assessment tools are used beyond the first few days after birth to assess development of infants, with many infants either discharged early or too sick to be assessed within the first few days after birth, it is important to establish reference data for infants who are greater than a few days old. Further, given that these assessment tools can be used from approximately 32 weeks' postmenstrual age, it is important to establish normative data for preterm infants prior to term-equivalent age. Normative data for neurobehavioural and neurological development of infants born preterm and healthy term born infants in the first weeks after birth are essential to understand the emergence of neurobehavioural and neurological development and to compare an individual infant's performance with a larger sample of infants born at similar gestations. This information can then be used to inform intervention and counsel parents appropriately.

The GMA is not based upon normative data, rather it involves a qualitative assessment of infants' spontaneous movement patterns, with movements classified as normal or abnormal [2,16,17]. The majority of the research to date on the GMA has focused on infants at high-risk of neurodevelopmental impairments, such as infants born very preterm or with brain injury [12,18]. Recent studies have shown that the rates of abnormal GMs in moderate-late preterm and healthy term born populations are lower than high-risk populations [19,20]. Importantly, both studies by Ploegstra et al. and Einspieler et al. report that GMA change character in the month post-term age, highlighting the importance of understanding GMA in typically developing infants and low-risk populations [19,20].

The aims of this study were to examine:

1. the expected range of values for three different neurobehavioural/neurological assessments (HNNE, NNNS, GMA) among moderate preterm (MPT: born 32^{+0} to 33^{+6}), late preterm (LPT: 34^{+0} to 36^{+6}) and term infants (FT: born 37 to 42 weeks' gestation) in the first weeks after birth, and
2. the effects of sex, gestational age at birth, and postmenstrual age at assessment on the different neurobehavioural/neurological assessments within all groups.

2. Methods

This prospective study involved MPT, LPT and FT infants born at the Royal Women's Hospital, Melbourne, Australia between November 2009 and March 2014. Infants were included if they had parents who could speak English (as funding was not available for interpreters) and did not have a congenital abnormality known to be associated with adverse outcomes. FT infants were excluded if they were admitted to the neonatal intensive or special care nursery. The study was approved by the hospital's Human Research Ethics Committee and parents provided written informed consent for their infant to participate in the study.

Perinatal data were recorded during the neonatal period by a research nurse and included gestation at birth, birthweight, small for gestational age, sex, mode of delivery, multiple birth, use of antenatal steroids, and respiratory distress at birth.

2.1. Neurobehavioural and neurological assessments

The infants were examined by one of six assessors (neonatologist, physiotherapist, occupational therapist or neonatal nurse) who were all certified in the NNNS and GMA. In comparison, the HNNE requires no formal certification; however the assessors completed training sessions with an experienced examiner, including reading the manual. Inter-rater reliability for the assessments has been previously reported for this cohort, with the majority of assessments having moderate to excellent reliability [15,21].

The three standardised neurobehavioural/neurological assessments were chosen because they provide complementary information regarding the infant's neurodevelopment [1,4]. The HNNE is a predominantly neurological exam [10], the NNNS [9] is a more neurobehaviourally focused assessment although it contains some neurological items and includes detailed items on the infant's behavioural responses, and the GMA is an assessment of neurological integrity requiring observation only of movements. The infants were examined in a hospital setting or during a home visit. The MPT and LPT infants were assessed between two days to two weeks after birth (i.e. prior to term- equivalent age), whilst the FT infants were assessed at term-equivalent age (38 to 44^{+6} weeks) with a wider range of two days to four weeks after birth. The term equivalent age assessments had a larger time frame to reflect clinical practice, where it is not always possible to assess an infant within the first few days after birth, especially in an outpatient setting.

Infants were assessed according to standardised assessment procedures, in a warm, quiet room, with the infants minimally dressed, and their parents or caregivers present. The NNNS and HNNE have several items that are administered in both examinations, such as grasp, palmar, rooting and moro reflexes, observation of spontaneous movements, tone patterns and head control. The procedure for the assessments involved the NNNS being administered first, followed by additional items needed to complete the HNNE (including arm and leg traction, head control one and two, and tendon reflexes), followed by the GMA [22].

2.2. Hammersmith Neonatal Neurological Examination (HNNE)

The HNNE is an assessment developed for term and preterm infants for use in the newborn period and has been validated for term-equivalent age [10,23,24]. It consists of 34 items, which assess neurological function across six categories including: tone, tone patterns, reflexes, spontaneous movements, abnormal neurological signs, and behaviour. Items are scored according to a five-point scale, with half scores appropriate if an item falls between categories. A half score can be given if an item its best described as fitting between two categories (i.e. a score of 3.5 can be given if the infant is performing between a 3 and 4). These scores are defined as raw scores. Optimality scores are then calculated because the raw scores are not linear, i.e. for most items a low score and a high score are both non-optimal, with a score around the middle considered optimal. For example, for the posture item, a score of 1–2 would indicate low tone, a score of 3 and 4 would be normal and a score of 5 would indicate high tone [10]. The overall optimality score (total score) was designed primarily for use in research and was originally validated on 224 low-risk term infants from England, who were assessed between six and 48 h following birth [3,10]. The distribution of the whole population was plotted for each item, and the 5th/95th and 10th/90th centiles were used as cut-offs, with a score between the 10th to 90th centile given a score of 1, scores between the 5th to 10th or 90th to 95th) given 0.5, and scores below/above the 5th/95th centile given a score of 0. The same approach for assigning optimality scores was used for the current study.

2.3. Neonatal Intensive Care Unit Network Neurobehavioural Scale (NNNS)

The NNNS is a comprehensive assessment of infant neurobehaviour and evaluates neurological integrity, behavioural function, and the presence of stress signs in newborn infants [9]. It was designed for use in research and clinical settings for infants at risk of neurobehavioural deficits due to prenatal drug exposure and/or prematurity and is recommended for use in infants from 34 to 48 weeks' postmenstrual age [26]. More recently, the NNNS has been used to describe normative neurobehaviour in 344 healthy term-born children assessed within the first 18 to 48 (mean age at testing 32.3 ± 13.6 h) hours of life, thus broadening its use [13]. The NNNS consists of 128 items, 45 items administered to the infant in a standardised, state dependent sequence, with further items scored (defined as raw scores) based upon observations throughout the examination. The NNNS raw scores are then converted to create 13 summary scales based upon conceptual and statistical grouping of items [26]. Summary scales include: habituation, attention, arousal, self-regulation, handling, quality of movement, excitability, lethargy, non-optimal reflexes, asymmetrical reflexes, hypertonicity, hypotonicity, and stress/abstinence. Higher scores on each of the scales represent more of the construct being measured, but higher scores for the attention, quality of movement, and regulation scales represent better neurobehavioural performance, whilst higher scores on handling, non-optimal reflexes, asymmetrical reflexes, hypotonicity, hypertonicity, excitability, lethargy, and the stress/abstinence scale represent poorer neurobehavioural performance [13]. For the arousal subscale scores, low scores indicate low levels of arousal, whilst high scores indicate too much arousal [27,28]. The habituation scale was excluded as infants were not consistently in an appropriate state (sleep) to administer the scale at the commencement of the assessment.

2.4. General Movements Assessment

Prechtl's method of qualitative assessment of general movements involves observation of an infant's spontaneous movement repertoire from birth (including preterm birth) up to six months of age post term [17]. GMA in both preterm and term born infants at risk of neurodevelopmental impairments due to a variety of perinatal risk factors have been shown to be predictive of a range of neurodevelopmental long-term outcomes, particularly cerebral palsy [12,16]. GMA were used to classify infant movements as normal or abnormal based upon three to five minutes of video footage of spontaneous movements in supine, without any stimulation and scored off-line at a later time point. Infants were classified as having normal writhing movements if they demonstrated movements that were complex, variable and fluent, whilst abnormal writhing movements included poor repertoire (monotonous and non-complex), cramped synchronised (all limbs and trunk movements contract simultaneously and appear rigid) or chaotic (large amplitude, chaotic order, without any fluency) [2].

2.5. Data analysis

Data were analysed using Stata 13.0, with results for each of the three gestational age groups reported separately (MPT, LPT and FT). For the HNNE the percentage of infants who performed in each category from 1-5 was calculated for each item score. From these results optimality scores for each item were calculated, as described above. The mean, standard deviation, range, and 5th, 10th, 25th, 50th, 75th, 90th and 95th percentile values for HNNE subscale optimality scores, and the NNNS summary scores are presented for each group. For the GMA the rates of infants classified as normal and abnormal (poor repertoire, chaotic, cramped synchronised) were reported for each group.

The relationships of sex, gestational age at birth and postmenstrual age at assessment, with the HNNE optimality scores, NNNS summary scores and GMA classifications were examined using linear regression for continuous data and logistic regression for categorical data.

3. Results

Overall 225 preterm and 201 FT infants were recruited. Neurobehavioural/neurological assessments were administered for 80 MPT, 129 LPT and 185 FT infants (Table 1). Of those with missing data, 11 FT infants were excluded because they were assessed >44^{+6} weeks, one FT infant was too unsettled to commence the assessment, and the remaining infants withdrew from the study after

Table 1
Characteristics of study sample.

Variable	MPT	LPT	Term
	N = 80	N = 129	N = 185
Birth weight (grammes) – mean (SD)	1887 (364)	2329 (450)	3534 (450)
Gestational age at birth (weeks) – mean (SD)	33.0 (0.6)	35.2 (0.8)	39.7 (1.2)
Postmenstrual age at exam (weeks) – mean (SD)	34.4 (0.8)	36.4 (0.9)	41.9 (1.5)
Chronological age at exam (weeks) – mean (SD)	1.2 (0.5)	1.3 (0.6)	2.2 (1.5)
Male – n (%)	38 (48)	64 (50)	97 (52)
Small for gestational age[a] – n (%)	8 (10)	12 (9)	0 (0)
Caesarean delivery – n (%)	55 (69)	79 (60)	71 (38)
Multiple birth – n (%)	35 (45)	35 (27)	1 (0.5)
Antenatal corticosteroids – n (%)	61 (76)	65 (50)	1 (0.5)
Respiratory distress at birth – n (%)	22 (28)	24 (19)	0 (0)

[a] Birthweight z-score < −2SD below the mean.

recruitment. Complete data were available for 50 MPT, 105 LPT and 165 FT infants for the HNNE, 65 MPT, 104 LPT and 153 FT infants for the NNNS, and 59 MPT, 101 LPT and 125 FT infants for the GMA. The remaining infants had assessments with incomplete data due to the infant being in an inappropriate state to assess or the examiner did not administer the item. The mean postmenstrual ages at assessment were 34.4 weeks (range 33 to 36 weeks) for the MPT group, 36.4 weeks (range 34 to 39 weeks) for the LPT group, and 41.9 weeks (range 38 to 42 weeks) for the FT group. The mean time since birth (i.e. chronological age) at assessment was 1.2 weeks (range 0.3 to 2.4 weeks) for MPT and 1.4 weeks (range 0.2 to 2.4 weeks) for LPT infants and 2.2 weeks (range 0.3 to 4.8 weeks) for FT infants. The perinatal characteristics of each gestational age group are described in Table 1.

3.1. HNNE

Overall the FT infants had higher raw scores for the HNNE items, with less variability than among infants born MPT or LPT, resulting in different cut-offs for the optimality scores across each gestational age group for each item. The only exception was for flexor posture, which was the same among all groups (Table 2). The optimality scores for all gestational age groups are represented in Table 3 and are based upon the distribution of raw scores obtained in Table 2. There were no significant relationships between sex, gestational age at birth, or age at time of assessment and the HNNE optimality scores for the subscales or the total score.

3.2. NNNS

The performance of infants across the NNNS was generally better for FT compared with MPT or LPT infants, with FT infants having higher mean and median scores for attention, quality of movement and less hypotonicity, excitability, non-optimal reflexes, lethargy and stress (Table 4). However, FT infants had higher mean and median scores for arousal, handling and asymmetrical reflexes. For infants born MPT and LPT, increased postmenstrual age at assessment was related to higher scores for handling, quality of movement, arousal and lower scores for hypotonicity and lethargy (Table 5). Further for infants born MPT and LPT, increased gestational age at birth was related to higher arousal and regulation scores and lower hypotonicity and lethargy (MPT only) scores. Gestational age was related to handling scores only for MPT infants. The only relationship with sex and the NNNS scores for preterm infants was for MPT infants and handling.

For infants born FT, males were more likely to have higher hypotonicity scores and lower attention and hypertonicity scores. Further for FT infants, increased postmenstrual age at time of assessment was related to higher attention scores and lower lethargy scores. There was little

Table 2
Hammersmith Neonatal Neurological Examination — raw scores and centiles for moderate, late and full term infants within the first month after birth.

GA at birth	Moderate preterm (32^{+0}–33^{+6})									Late preterm (34^{+0}–36^{+6})									Term (37^{+0}–41^{+6})								
Tone patterns																											
Score	1	1.5	2	2.5	3	3.5	4	4.5	5	1	1.5	2	2.5	3	3.5	4	4.5	5	1	1.5	2	2.5	3	3.5	4	4.5	5
Posture	11	0	31	5	36	4	12	0	0	3	1	20	5	39	4	27	0	1	0	0	3	1	28	5	62	0	1
Arm recoil	12	1	33	3	21	3	27	0	0	8	1	27	1	18	2	43	0	0	3	0	8	2	21	2	63	0	1
Arm traction	13	10	53	1	19	2	2	0	0	7	2	41	5	34	2	9	0	0	0	0	9	1	36	7	46	0	1
Leg recoil	6	0	15	2	12	0	65	0	0	1	0	9	1	7	1	81	1	0	1	0	3	2	10	2	83	0	0
Leg traction	4	3	45	4	29	4	10	1	0	1	2	23	6	42	2	20	1	3	0	0	2	2	13	7	74	2	0
Popliteal angle	36	5	39	13	6	0	1	0	0	17	2	42	17	16	1	5	0	0	1	1	2	33	42	7	13	0	1
Head control 1	24	1	36	1	27	3	8	0	0	13	2	45	2	29	2	7	0	0	1	1	10	3	45	3	37	0	0
Head control 2	22	0	26	0	47	1	4	0	0	10	2	31	2	42	1	12	0	0	1	1	8	3	47	3	36	0	1
Head lag	33	3	32	3	20	1	8	0	0	22	4	35	3	28	0	8	0	0	2	1	28	2	42	1	23	0	0
Ventral suspen	33	7	37	1	16	1	3	0	1	12	2	47	3	29	2	4	0	1	1	1	16	5	65	2	10	0	0
Flexor traction	0	0	54	0	43	0	3	0	0	0	0	52	0	41	0	7	0	0	0	0	38	0	57	0	4	0	1
Flexor posture	0	0	1	0	98	0	1	0	0	0	0	3	0	96	0	1	0	0	0	0	0	0	98	0	2	0	0
Leg tone	0	0	11	0	26	0	39	0	24	0	0	9	0	26	0	42	0	23	0	0	7	2	19	0	48	1	23
Neck tone	0	0	23	0	57	0	17	0	3	0	0		0	59	0	11	0	1	0	0	11	0	80	0	9	0	0
Ext tone	0	0	24	0	61	0	14	0	1	0	0	23	0	50	0	23	0	4	1	0	23	0	53	1	20	0	2
Reflexes																											
Tendon	1	0	3	0	83	0	3	0	0	0	0	13	1	83	1	2	0	0	1	0	7	0	89	1	2	0	1
Sucking	8	0	48	5	18	1	19	0	1	2	0	15	2	31	4	46	0	1	1	0	3	0	9	3	83	1	0
Palmer grasp	0	0	66	1	32	0	1	0	0	2	1	49	2	41	0	4	0	0	0	0	16	4	52	1	26	0	0
Plantar grasp	0	0	26	0	74	0	0	0	0	0	0	20	2	77	0	0	0	0	1	0	4	1	94	0	0	0	0
Moro	0	1	29	6	34	1	9	1	19	2	0	18	1	40	6	14	0	19	3	1	3	0	34	7	48	1	3
Placing	17	4	30	5	43	0	1	0	0	13	0	33	3	51	0	0	0	0	7	1	28	4	60	0	0	0	0
Spontaneous movements																											
Quality	1	1	26	4	30	9	28	0	1	1	0	18	3	23	15	38	0	2	0	0	2	0	4	2	91	1	0
Quantity	0	0	16	1	26	6	49	0	2	0	0	7	1	23	10	57	0	2	0	0	1	0	3	2	93	1	0
Head raising	27	1	37	0	17	0	16	0	1	10	2	37	2	21	0	27	0	2	0	0	22	1	22	1	50	1	3
Abnormal signs																											
Hand posture	0	0	62	1	36	0	0	0	1	1	0	65	1	32	0	0	0	1	0	0	69	1	28	0	2	0	0
Tremors	0	0	26	0	41	1	32	0	0	0	0	27	9	49	4	18	0	4	0	0	68	0	26	1	5	0	0
Startles	1	0	44	0	43	0	12	0	0	2	0	54	1	34	0	9	0	0	5	0	70	5	16	0	3	0	1

Table 2 (*continued*)

GA at birth	Moderate preterm (32^{+0}–33^{+6})									Late preterm (34^{+0}–36^{+6})									Term (37^{+0}–41^{+6})								
Behaviour																											
Eyes	10	0	1	0	67	1	20	0	1	14	0	1	0	73	1	11	0	0	4	0	0	0	93	0	3	0	0
Auditory orient	17	0	48	3	32	0	0	0	0	18	1	47	2	32	0	0	0	0	4	0	19	2	46	3	26	0	0
Visual orient	18	0	43	1	14	3	21	0	0	16	0	39	2	13	3	24	0	3	7	0	11	1	7	4	62	1	7
Alertness	10	0	37	1	51	0	1	0	0	10	2	26	2	52	2	6	0	0	2	0	11	1	45	8	33	0	0
Irritable	24	1	69	3	2	0	0	0	1	8	2	60	1	24	1	4	0	0	8	0	50	1	37	0	4	0	3
Cry	24	0	14	0	61	0	0	0	1	6	1	5	0	87	0	1	0	0	8	0	1	0	88	1	0	0	2
Console	26	0	50	0	23	0	1	0	0	8	2	50	0	29	3	8	0	0	9	1	25	0	28	2	35	0	0

Note: Dark shading indicates scores in the optimal range (10-90th centile), light shading indicates scores in the suboptimal range (5th-10th centile or 90-95th centile) and no shading indicates non-optimal scores (<5th centile or >95th centile). Box with black outline represents the median score.

evidence of a relationship between gestational age at birth and NNNS scores for the FT infants.

3.3. GMA

The rates of normal GMA were 25% for infants born MPT, 32% for LPT and 90% for FT infants (Table 6). For infants born MPT, there was a decreasing odds ratio for abnormal GMA with increasing gestational age at birth (odds ratio 0.20; 95% CI 0.06 to 0.67), but not for the other gestational age groups. In addition, for infants born MPT, there was a decreasing odds ratio for abnormal GMA with increasing postmenstrual age at assessment (odds ratio 0.23; 95% CI 0.08 to 0.64), but not for the other gestational age groups. There was little evidence of a relationship between sex and GMA for any gestational age groups.

4. Discussion

This study provides reference data for samples of MPT, LPT and FT infants for three neurobehavioural/neurological assessments, the HNNE, NNNS and GMA administered in the first weeks after birth. An important role of a standardised examination is to provide norms against which to judge the performance of a group with a particular characteristic (e.g. prematurity) or an individual [26]. For all three assessments these data provide a reference for infants that may require further investigation or closer surveillance, however, the data cannot be used for diagnosis of a neurological abnormality. Whilst the three assessments have the same goal of identifying children at-risk of longer-term neurodevelopmental impairments, and share many common elements grounded in pioneering work in neonatal neurology, the tools differ in the information they provide to the clinician [3]. The HNNE gives an overall optimality score, with the range of scores being quite narrow for FT infants, but broader for infants born MPT or LPT. Whilst one or more item scores in the non-optimal range was common in all groups, Dubowitz et al. emphasize that the overall score is more important for determining whether further investigations are required [10]. The GMA assessment also gives an overall classification, with movements described as normal or abnormal, but does not require any handling of the infant. Infants born FT were more likely to have normal GMA, with only 10% of infants having abnormal GMA, compared with 75% of MPT and 68% of LPT infants. Whilst the GMA provide an overall

Table 3
Hammersmith Neonatal Neurological Examination optimality scores for moderate, late and full term infants within the first month after birth.

Optimality scores	GA at birth	N	Mean	SD	Range	5th	10th	25th	50th	75th	90th	95th
Tone subscale	MPT	77	8.52	1.28	4.5–10	5.9	6.5	7.8	9.0	9.5	10	10
	LPT	127	8.92	0.98	5.5–10	7.0	7.5	8.5	9.0	9.	10	10
	FT	181	9.15	1.18	4.0–10	6.6	7.6	8.5	9.5	10	10	10
Tone patterns subscale	MPT	75	4.35	0.50	3.0–5	3.4	3.8	4.0	4.5	4.5	5.0	5.0
	LPT	127	4.45	0.65	1.5–5	3.0	3.5	4.0	4.5	5.0	5.0	5.0
	FT	177	4.56	0.44	2.5–5	4.0	4.0	4.5	4.5	5.0	5.0	5.0
Reflexes	MPT	51	5.56	0.53	3.5–6	5.3	5.0	5.5	5.5	6.0	6.0	6.0
	LPT	110	5.28	0.71	3.5–6	4.0	4.1	5.0	5.5	6.0	6.0	6.0
	FT	170	5.61	0.60	2.5–6	4.5	5.0	5.5	6.0	6.0	6.0	6.0
Spontaneous Movements	MPT	75	2.50	0.67	1.0–3	1.0	1.0	2.5	3.0	3.0	3.0	3.0
	LPT	127	2.72	0.50	0.5–3	1.5	2.0	2.5	3.0	3.0	3.0	3.0
	FT	182	2.77	0.44	0.5–3	2.0	2.0	2.5	3.0	3.0	3.0	3.0
Abnormal signs	MPT	79	2.91	0.22	2–3	2.5	2.5	3.0	3.0	3.0	3.0	3.0
	LPT	127	2.81	0.37	1–3	2.0	2.4	2.5	3.0	3.0	3.0	3.0
	FT	182	2.79	0.37	1–3	2.0	2.5	2.5	3.0	3.0	3.0	3.0
Behaviour	MPT	75	6.19	1.52	3–7	4.0	5.0	6.0	6.5	7.0	7.0	7.0
	LPT	122	6.20	1.09	3–7	3.5	5.0	5.9	6.5	7.0	7.0	7.0
	FT	179	6.09	0.99	2–7	4.0	4.5	6.0	7.0	7.0	7.0	7.0
Total score	MPT	50	30.40	2.43	22–33	24.6	27.5	28.9	31.5	32.0	32.5	33.0
	LPT	105	30.42	2.62	23–34	25.0	25.3	29.0	31.0	32.5	33.0	33.5
	FT	165	31.14	2.29	21–34	26.7	28.5	30.5	32.0	33.0	33.5	34.0

MPT = moderate preterm term; LPT = late preterm; FT = full term.

Table 4
NICU Network Neurobehavioural Scale mean, standard deviation and centiles for moderate, late and full infants within the first month after birth.

Scale	GA at birth	N	Mean	SD	Range	5th	10th	25th	50th	75th	90th	95th
Attention	MPT	65	4.03	1.14	1.29–6.71	1.54	2.66	3.34	4.00	7.76	5.43	6.01
	LPT	99	4.35	1.21	2.00–6.86	2.43	2.71	3.29	4.29	5.29	6.00	6.57
	FT	153	5.85	1.32	2–8.7	3.43	4.00	5.00	5.86	6.86	7.42	7.90
Handling	MPT	67	0.35	0.26	0–1	0	0	0.13	0.38	0.63	0.75	0.75
	LPT	104	0.43	0.35	0–1	0	0.13	0.13	0.38	0.75	0.81	0.88
	Term	164	0.49	0.29	0–1	0	0	0.25	0.50	0.75	0.88	0.88
Quality of movement	MPT	77	4.18	0.58	2.50–5.67	3.13	3.33	3.67	4.00	4.79	5.23	5.50
	LPT	122	4.43	0.66	2.83–5.50	3.30	3.50	4.00	4.50	5.00	5.33	5.50
	Term	180	5.00	0.66	2.8–6.2	4	4.16	4.67	5.17	5.48	5.66	5.83
Arousal	MPT	77	3.17	0.63	1.83–5.43	2.13	2.43	2.71	3.14	3.57	4.00	4.01
	LPT	123	3.63	0.65	1.71–5.14	2.46	2.86	3.14	3.71	4.00	4.51	4.83
	Term	180	3.92	0.67	2–5.7	3	3.01	3.43	3.86	4.29	4.84	5.14
Regulation	MPT	73	5.04	0.94	2.55–6.71	3.33	3.61	4.20	5.31	5.74	6.15	6.32
	LPT	120	5.31	0.81	3.38–7.29	3.72	4.14	4.60	5.24	5.85	6.32	6.62
	Term	180	5.91	0.87	3.4–7.9	4.40	4.80	5.33	5.93	6.53	7.08	7.29
Hyper tonicity	MPT	77	0.03	0.16	0–1	0	0	0	0	0	0	1.00
	LPT	123	0.04	0.20	0–1	0	0	0	0	0	0	1.00
	Term	180	0.08	0.34	0–3	0	0	0	0	0	0	1.00
Hypo tonicity	MPT	77	2.06	1.49	0–6	0	0	1.00	2.00	3.00	4.00	5.10
	LPT	123	1.06	1.28	0–5	0	0	0	1.00	1.00	3.00	4.00
	Term	180	0.23	0.49	0–3	0	0	0	0	0	0	1.00
Asymmetric reflexes	MPT	77	1.22	1.17	0–4	0	0	0	1.00	2.00	3.00	3.00
	LPT	123	1.33	1.26	0–6	0	0	0	1.00	2.00	3.00	4.00
	Term	180	4.17	2.18	0–10	1.00	1.00	2.00	4.00	6.00	7.00	8.00
Excitability	MPT	77	4.1	2.4	0–9	0	0	1.00	2.00	3.00	4.00	5.20
	LPT	123	2.69	2.00	0–9	0	0	1.00	3.00	4.00	5.00	6.80
	Term	180	2.13	2.11	0–8	0	0	0	2.00	3.00	5.90	6.95
Non-optimal reflexes	MPT	77	6.90	2.28	1–12	3.00	4.00	5.50	7.00	8.00	10.0	10.1
	LPT	123	6.29	2.38	1–12	2.00	3.00	4.00	6.00	8.00	9.00	11.0
	Term	180	0.80	0.98	0–7	0	0	0	1.00	1.00	2.00	2.00
Lethargy	MPT	77	7.44	3.61	0–15	2.00	3.00	5.00	7.00	10.5	13.0	13.1
	LPT	123	6.01	3.28	0–15	2.00	2.00	3.00	5.00	9.00	10.6	11.8
	Term	180	3.90	2.06	0–13	2.00	2.00	3.00	4.00	4.00	6.00	8.95
Stress	MPT	77	0.17	0.06	0.04–0.33	0.10	0.10	0.12	0.16	0.20	0.24	0.27
	LPT	122	0.14	0.05	0.03–0.37	0.06	0.07	0.10	0.14	0.17	0.20	0.22
	Term	180	0.08	0.06	0–0.4	0.02	0.02	0.04	0.06	0.10	0.16	0.18

classification, the other examinations may help to determine what the focus of the monitoring or intervention might be for an infant and family, such as a focus on tone, handling strategies, or visual orientation. The NNNS on the other hand does not provide an overall summary score, rather it provides information on 13 scales of different neurobehavioural constructs. The NNNS range of scores was also larger for infants born early compared with FT infants, with FT infants having better attention, quality of movement, hypotonicity, excitability, non-optimal reflexes, lethargy and stress. This information is particularly useful for evaluating neurobehavioural interventions, with the NNNS shown to be sensitive to change in several intervention studies [29–31].

Similar to our study findings, a study of 380 preterm infants born between 25 to 35 weeks' gestation and assessed with the HNNE at term equivalent age had a broader range of responses than peers born at

Table 5
NICU Network Neurobehavioural Scale and relationship with sex, gestational age and postmenstrual age.

Group	Variable	Handling[b]	Quality of movement	Arousal	Regulation	Hypotonicity[b]	Lethargy[b]	Attention
		Mean (95%CI)						
MPT	GA[a]	0.12 (0.02 0.22)		0.37 (0.14, 0.59)	0.45 (0.10, 0.80)	−1.36 (−1.83, −0.89)	−2.14 (−3.14, −0.85)	
	PMA[a]	0.12 (0.04, 0.19)	0.18 (0.03, 0.44)	0.25 (0.08, 0.42)	0.31 (0.04, 0.58)	−0.81 (−1.21, −0.43)	−0.81 (−1.21, −0.43)	
	Male	−0.13 (−0.25, 0.01)						
LPT	GA			0.21 (0.08, 0.35)	0.26 (0.09, 0.43)	−0.45 (−0.73, −0.18)		
	PMA	0.07 (0.0, 0.14)	0.18 (0.04, 0.32)	0.16 (0.02, 0.30)	0.28 (0.11, 0.45)	−0.44 (−0.71, −0.17)	−1.36 (−2.36, −0.35)	
	Male							
FT	GA							
	PMA						−0.27 (−0.41, −0.12)	0.26 (0.07, 0.50)
	Male					0.15 (0.00, 0.29)		−0.42 (−0.84, −0.01)

MPT = moderate preterm; LPT = late preterm; FT = full term; GA = gestational age; PMA = post menstrual age.
[a] Per one week's increase.
[b] Lower scores are better.

Table 6
General movements for moderate, late and full infants within the first month after birth.

Normal n (%)		Abnormal			Total
		PR n (%)	CS n (%)	Ch n (%)	
MPT	15 (25)	43 (73)	1 (2)	0	59
LPT	32 (32)	69 (68)	0	0	101
FT	112 (90)	13 (10)	0	0	125

MPT = moderate preterm; LPT = late preterm; FT = full term; PR = poor repertoire; CS = cramped synchronised; Ch = chaotic.

term [24]. Whilst our study assessed the preterm infants earlier, within the first few weeks after birth, we also found that preterm infants had less trunk and leg flexor tone, and poorer head control and quality of movement compared with term born infants. On the NNNS, preterm infants have been reported to have poorer arousal, regulation, and quality of movement, and higher rates of non-optimal reflexes and hypotonicity when assessed at term [25,27]. Whilst we also found that preterm infants had lower arousal scores than FT infants, it should be noted that several authors have suggested that both low and high scores on this subscale may be of concern and thus caution should be taken when interpreting this subscale as a continuous variable [13,27]. It will be important to understand if these differences in neurobehaviour within the first few weeks after birth between preterm and term born infants are predictive of longer-term outcomes.

Of importance to clinical and research findings, the HNNE optimality scores were not affected by gestational age at birth, age at assessment, or sex, whilst there were several relationships between NNNS scores and gestational age at birth, postmenstrual age at assessment and sex. However, for the GMA, gestational age at birth and postmenstrual age at assessment were only important for those born MPT. These differences in relationships with gestational age and postmenstrual age at assessment may be due to the HNNE and GMA having a more neurological focus, which is more likely to be consistent over the first few weeks after birth, whilst the NNNS has more of a behavioural focus, which is sensitive to changes with the experience of the infant, not only in the postnatal period but also due to prematurity. This may be of importance when determining assessments to compare differences in performance between groups, as it appears the NNNS may have more ability to detect differences across groups in many domains. These findings are consistent with Romeo et al. [32] who reported HNNE scores were not related to age at examination in LPT infants assessed within the first three days after birth, whilst Fink et al. also found that gestational age, sex, and the age of the newborn at testing affected neurobehavioural performance on the NNNS [13]. Further, several authors have reported that that increasing gestational age at birth and postmenstrual age at assessment have a positive relationship with GMA in infants born very preterm and FT, with Einspieler et al. reporting that GMA change character again in the first month post term age [15,19].

Neurobehavioural/neurological assessments can be useful for referring infants for early intervention; of note, the current study demonstrates the importance of having normative data for different gestational ages, as there is a wide range of variability in scores. However, there are some limitations to the study. There was a wider range of time post birth that data were collected in the current study compared with previous studies. Whilst the aim of this study was to assess neurobehaviour and neurological function in the first few weeks after birth, due to difficulty of timing outpatient assessments for newborn infants in research studies, the age range was from two days to two weeks for the preterm infants and two days to four weeks for the term infants. However, this does reflect clinical practice and provide a larger reference range for comparison. The normative data provided in this study represent a cohort of infants recruited from a tertiary hospital in Australia, which may limit generalisability to other cultural contexts. Further, the predictive value for longer-term outcomes of all three assessments using the reference values in this cohort has not been determined.

In conclusion, this paper presents normative data for samples of MPT, LPT and FT infants assessed with three neurobehavioural/neurological assessments, from a few days to a few weeks after birth. Future research examining the long-term predictive value of the HNNE optimality scores, NNNS cut-off scores and GMA for the MPT, LPT and FT infants is needed, not only to determine the validity of these assessments prior to term, but also for FT infants from different cultural backgrounds and at later postmenstrual ages than previous reference data.

Conflict of interest statement

No conflict of interest declared.

Acknowledgements

This study was funded by grants from the National Health and Medical Research Council (Project Grant ID 1024516 and 1028822, Early Career Fellowships ID 1053767-AJS and ID 1053787-JLYC, Research Fellowship ID 1081288-PJA); Centre of Research Excellence in Newborn Medicine ID 1060733; Co-funded Australian Postgraduate Association Scholarship, University of Melbourne/Postgraduate Health Research Scholarship, Murdoch Childrens Research Institute (JEO), and the Victorian Government's Operational Infrastructure Support Program.

References

[1] Brown NC, Spittle AJ. Neurobehavioral evaluation in the preterm and term infant. Curr Pediatr Rev 2014;10(1):65–72.
[2] Einspieler C, Prechtl HF. Prechtl's assessment of general movements: a diagnostic tool for the functional assessment of the young nervous system. Ment Retard Dev Disabil Res Rev 2005;11(1):61–7 (P).
[3] Wusthoff C. How to use: the neonatal neurological examination. Arch Dis Child Educ Pract Ed 2013;98(4):148–53.
[4] El-Dib M, Massaro AN, Glass P, Aly H. Neurodevelopmental assessment of the newborn: an opportunity for prediction of outcome. Brain Dev 2011;33(2):95–105.
[5] Miller MQ, Quinn-Hurst M. Neurobehavioral assessment of high-risk infants in the neonatal intensive care unit. Am J Occup Ther 1994;48(6):506–13.
[6] El-Dib M, Massaro AN, Glass P, Aly H. Neurobehavioral assessment as a predictor of neurodevelopmental outcome in preterm infants. J Perinatol 2012;32(4):299–303.
[7] Spittle AJ, Spencer-Smith MM, Cheong JL, Eeles AL, Lee KJ, Anderson PJ, et al. General Movements in very preterm children and neurodevelopment at 2 and 4 years. Pediatrics 2013 Jul;22.
[8] Liu J, Bann C, Lester B, Tronick E, Das A, Lagasse L, et al. Neonatal neurobehavior predicts medical and behavioral outcome. Pediatrics 2010;125(1):e90–8.
[9] Lester BM, Tronick EZ, Brazelton TB. The Neonatal Intensive Care Unit network neurobehavioral scale procedures. Pediatrics 2004;113(3 Pt 2):641–67.
[10] Dubowitz L, Mercuri E, Dubowitz V. An optimality score for the neurologic examination of the term newborn. J Pediatr 1998;133(3):406–16.
[11] Noble Y, Boyd R. Neonatal assessments for the preterm infant up to 4 months corrected age: a systematic review. Dev Med Child Neurol 2012;54(2):129–39.
[12] Bosanquet M, Copeland L, Ware R, Boyd R. A systematic review of tests to predict cerebral palsy in young children. Dev Med Child Neurol 2013;55(5):418–26.
[13] Fink NS, Tronick E, Olson K, Lester B. Healthy newborns' neurobehavior: norms and relations to medical and demographic factors. J Pediatr 2012;161(6):1073–9.
[14] Pineda RG, Castellano A, Rogers C, Neil JJ, Inder T. Factors associated with developmental concern and intent to access therapy following discharge from the NICU. Pediatr Phys Ther 2013;25(1):62–9.
[15] Olsen J, Brown N, Eeles A, Lee K, Anderson P, Cheong J, et al. Trajectories of general movements from birth to term-equivalent age in infants born <30 weeks' gestation. Early Hum Dev 2015;91(12):683–8.
[16] Prechtl HF, Einspieler C, Cioni G, Bos AF, Ferrari F, Sontheimer D. An early marker for neurological deficits after perinatal brain lesions. Lancet 1997;10;349(9062):1361–3.
[17] Einspieler C, Prechtl HF, Bos A, Ferrari F, Cioni G. Prechtl's method on the qualitative assessment of general movements in preterm, term and young infants. London: Mackeith Press; 2004.
[18] Darsaklis V, Snider LM, Majnemer A, Mazer B. Predictive validity of Prechtl's method on the qualitative assessment of general movements: a systematic review of the evidence. Dev Med Child Neurol 2011;53(10):896–906.
[19] Einspieler C, Marschik PB, Pansy J, Scheuchenegger A, Krieber M, Yang H, et al. The general movement optimality score: a detailed assessment of general movements during preterm and term age. Dev Med Child Neurol 2015 (e-pub agead of print).
[20] Ploegstra WM, Bos AF, de Vries NK. General movements in healthy full term infants during the first week after birth. Early Hum Dev 2014 Jan;90(1):55–60.
[21] Eeles A, Olsen J, McInnes E, Walsh J, Cheong J, Doyle LW, et al. Reliability of neurobehavioural assessments both preterm and at term. Phys Occup Ther Pediatr
[22] Spittle AJ, Thompson DK, Brown NC, Treyvaud K, Cheong JL, Lee KJ, et al. Neurobehaviour between birth and 40 weeks gestation in infants born <30 weeks

gestation and parental psychological wellbeing: predictors of brain development and child outcomes. BMC Pediatr Apr. 24 2014;14(1):111.
[23] Dubowitz L, Ricciw D, Mercuri E. The Dubowitz neurological examination of the full-term newborn. Ment Retard Dev Disabil Res Rev 2005;11(1):52–60.
[24] Ricci D, Romeo DMM, Haataja L, van Haastert IC, Cesarini L, Maunu J, et al. Neurological examination of preterm infants at term equivalent age. Early Hum Dev 2008; 84(11):751–61.
[25] Boukydis CFZ, Bigsby R, Lester BM. Clinical use of the Neonatal Intensive Care unit network neurobehavioral scale. Pediatrics 2004;113(3 Pt 2):679–89.
[26] Lester BM, Tronick EZ, Brazelton TB. The Neonatal Intensive Care unit network neurobehavioral scale procedures; Appendix 3: summary score calculations. Pediatrics 2004;113(3):695–9.
[27] Brown NC, Doyle LW, Bear MJ, Inder TE. Alterations in neurobehavior at term reflect differing perinatal exposures in very preterm infants. Pediatrics 2006;118(6):2461–71.
[28] Tronick E, Lester BM. Grandchild of the NBAS: the NICU network neurobehavioral scale (NNNS): a review of the research using the NNNS. J Child Adolesc Psychiatr Nurs 2013;26(3):193–203 (25).
[29] Lester BM, Hawes K, Abar B, Sullivan M, Miller R, Bigsby R, et al. Single-family room care and neurobehavioral and medical outcomes in preterm infants. Pediatrics 2014 Oct;134(4):754–60.
[30] Smith LM, LaGasse LL, Derauf C, Grant P, Shah R, Arria A, et al. The infant development, environment, and lifestyle study: effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. Pediatrics 2006 Sep; 118(3):1149–56.
[31] Barros MC, Mitsuhiro S, Chalem E, Laranjeira RR, Guinsburg R. Neurobehavior of late preterm infants of adolescent mothers. Neonatology 2011;99(2):133–9.
[32] Romeo DM, Luciano R, Corsello M, Ricci D, Brogna C, Zuppa A, et al. Neonatal neurological examination of late preterm babies. Early Hum Dev 2013;89(8):537–45.