Differences and Relations Between Chrono-Biological and Motor-Functional Characteristics of Infants

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Keywords: Muscle Tone, Neurodevelopment, Jaundice, Infants, Obstetric Mode of Delivery.

Abstract: Differences and relationships between chrono-biological (body weight-BW, body length-BL, gestational age-GA) and motor-functional characteristics (e.g., muscle tone) of infants with relation to different obstetric mode of delivery and jaundice were analysed. The assessment of muscle tone is an integral part of neuromotor evaluation. The study included 179 infants of both genders (AS±SD: age 158,36±110,91 days; BW 3267,78±708,69 grams; and BL of 49,33±3,09 cm) due to muscle tone disorders with the presence of mild and moderate neurodevelopmental disorders as a sequelae of immature brain impairment. Study revealed statistically significant differences in chrono-biological variables depending upon the different obstetric mode of delivery (BW, BL, and GA), as well upon neonatal jaundice (BW, BL, and possibly GA). Also, there is a statistically significant correlation among chrono-biological variables (BW, BL, GA: 0,62-0,88). When compared to infant's age at first physiatrist examination (AFE), individually and combined with GA, correlations imply importance of further inter-parametrial insights – in this case with relation to muscle tone classified in 4 groups (normal-, hypo-, hyper-, and changing-). Findings confirm statistically significant differences between infants differently categorized by muscle tone and infant's AFE- among hypertonic and hypotonic infants as well among hypertonic and alternating ones respectively. Although there are no correlations between the AFE with BW, BL (with GA they are very little correlated – 0,19), there is an indication that the existing categorization by tone demands more frequent or earlier 'screening' - embedded into existing communication for a balanced development overall.

1 INTRODUCTION

The assessment of muscle tone is an integral part of the routine neuromotor evaluation of new-borns, infants and children. Observation of a fluctuation in muscle tone aids in setting up a diagnosis, is used as justification for therapeutic approach, and is considered as an indicator of neurological change (Kathrein, 1990). It is well-known that many infants show one or two signs of atypical neuromotor performance, and that, generally, only an aggregation of multiple signs of atypical neuromotor performance is associated with elevated risk of neurodevelopmental disorders (Hadders-Algra et al., 2010). We addressed the alteration of muscle tone in infants and described the functional characteristics of muscle tone as follows: lowered (hypotonia), increased (hypertonia), changing muscle tone and normal mostly of a central etiology which happens to emerge antenatally, intrapartum, or postnatally. Muscle tone alterations are often represented in the so-called "risky children" (children who were exposed to one or more risk factors for neurodevelopmental disorders in their medical history), and those can be an implication of a primary disorder of the central nervous system (CNS) in terms of a prior brain disturbances (Lindahl et al., 1988). The changed muscle tone in terms of hypotonia, hypertonia and changing muscle tone is considered to be a symptomatic risk and it stands in need for the proper and prompt habilitation treatment, even though the spontaneous normalization is often achievable (Lazić et al., 2011). Thus, obtaining a comprehensive medical history is crucial in

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Marunica Karšaj, J. and Gruić, I.
Differences and Relations Between Chrono-Biological and Motor-Functional Characteristics of Infants.
DOI: 10.5220/0012268300003587
In *Proceedings of the 11th International Conference on Sport Sciences Research and Technology Support (icSPORTS 2023)*, pages 237-246
ISBN: 978-989-758-673-6; ISSN: 2184-3201

consolidation the extensive list of differential diagnoses due to muscle tone alternations. Worldwide shortly after birth, more than 80% of all term and late preterm infants develop some extent of neonatal jaundice or hyperbilirubinemia (Keren et al., 2008). Many studies pointed out that the GA was significantly associated to jaundice. It has been described that the risk of jaundice significantly heightens with lowering GA (Sarici et al., 2004). Moderate jaundice turned out to be linked with a significant increase in minor neuromotor disorder throughout the infancy (Soorani-Lunsing et al., 2001). Further inspections of muscle tone may be assessed within sEMG approach (presented in e.g.(Cifrek et al., 2021).

Bobaths' methodology gave definition on muscle tone as "the speed and the degree of resistance to passive external manipulation of the extremities for a period of time without interfering with length. It is a function of the tactile, vestibular and proprioceptive arrangement enabling an individual to preserve body posture against the pull of gravity in a resting position- static as well as the attainment of movement patterns-dynamic" (Bobath K, 1984). So, tone is defined as the resistance of muscles to stretch; therefore, hypotonia is diminished resistance of muscles to passive stretching (Crawford, 1992). However, a more appropriate definition of hypotonia is an impairment of the ability to sustain postural control and movement against gravity. Thus, floppy infants exhibit poor control of movement with prolonged head lag within arm pull test, procrastinated motor skills, and hypotonic motor movement patterns. The atypical motor patterns consist of alterations in postural control, increased range of motion of joints, and inadequate stability and movement biomechanics (Peredo et al., 2009). The critical feature of hypotonia refers to head and neck control. Mild or benign head lag is a common finding in new-borns and generally resolves by itself; however, the presence of severe relentless head lag beyond three to four months of age typically points to disorders related to hypotonia and muscle weakness in infancy (Linder et al., 1998). On the other hand, hypertonia is defined as an irregularly high resistance at the time of externally imposed passive movement. Increased muscle tone is usually characterized by stiff and inflexible muscles which happen to be hardly stretched, difficulty in moving from one position to another, involuntary crossing of lower extremities when lifted vertically, abrupt tremors or jerks which aggravate during periods of stress, coordination deficiency and delay in motor skills maturation. It is associated with opisthotonus which is assigned to aberrant axial extension and arching of the trunk produced by excessive contractions of the paraspinal musculature (Sanger et al., 2003). Recurrence-wise, hypertonia is less common in infants than hypotonia (Sanger et al., 2003).

Final goal of this research is to analyse and recognize differences between infants differently categorized by muscle tone and infant's AFE (normal-, hypo-, hyper-, and changing-), correlations among chrono-biological variables, differences in chrono-biological variables depending upon the different obstetric mode of delivery and neonatal jaundice.

2 METHODS

2.1 Sample of Entities

The sample of entities is comprised of 179 infants in age of 158,36±110,91 days at first physiatrist examination (as inclusion criterion), with BW 3267,78±708,69 grams and BL of 49,33±3,09 cm, without special exclusion criterion.

2.2 Sample of Variables

Anthropometric measures and data from antenatal, intrapartum and postnatal history were obtained on the first visit either based upon parental report or collected from documented medical history. Sample of variables is comprised of 3 independent (grouping) variables– tone (normal-, hypo-, hyper-, changing), jaundice (yes/no), birth delivery technique (spontaneously throughout birth canal/Caesarean section-CS), and 5 item battery of dependent variables, 4 basic and one derived – BW (grams), BL (cm), GA (days), AFE (days), GA and first examination summed (days).

2.3 Experimental Design

A series of comparisons of (two) independent variables (groups) were performed. The set of dependent variables covers chrono-biological characteristics of entities at birth, with age when first physiatrist examination was added. The set of grouping variables was determined by obstetric modes of delivery, jaundice, and muscle tone. The study included infants of both genders, aged 0-24 months, who were examined by a physiatrist due to the muscle tone disorders with the presence of mild and moderate neurodevelopmental signs and symptoms as a sequelae of immature brain lesion. The

modality of habilitation was prescribed corresponding to infant's clinical indication. Due to experience follow up shows those infants predominantly accomplished normal muscle tone and typical development in further childhood. Our study is the result of the continuous monitoring of the development assessed by physical examination of infants who were at risk due to their antenatal, intrapartum and postnatal medical history. Monitoring was carried out methodically, and a physiatrist examination was conducted in the outpatient polyclinic of the University Department of Rheumatology, Physical Medicine, and Rehabilitation.

While assessing muscle tone, an infant should be alert and relaxed but not sobbing. Extremity tone is readily assessed by externally imposed passive movements. Muscle tone is clinically evaluated by observation, and palpation during passive examination of the range of movement of appendicular and peripheral skeleton. Observation gives insight into both the global posture of the body and the acquirement and maintenance of the antigravity position in the supine and prone position of an infant. Besides examination is performed separately in the nuchal, truncal region and on the upper and lower extremities. In the neck, muscle tone is evaluated when testing resistance during passive rotation of the head to the right and left side. The muscle tone in the shoulder girdle is done by anteflexion with elevation and adduction of the flexed arm to the opposite shoulder ("scarf sign"); on the upper extremities' pronation and supination, flexion of the wrist, opening of the hands. Passive examining of the flexion and lateral flexion of the truncal region is also involved. Hip flexion, hip abduction and adduction, knee extension and flexion and foot dorsiflexion are passively examined on the lower extremities. Besides the engagement of locomotor system to assess muscle tone, inevitably are observed the expression of the infant's face, making eye contact, social smile and cry, the way of reacting to auditory, visual stimulus and qualitatively how infant initiates and performs movement (Goo et al., 2018).

Truncal and nuchal muscle tone may be best examined using arm traction test, horizontal and vertical suspension tests. In assessing arm traction test in supine position no head lag is expected after the age of three months. On vertical suspension, a healthy infant should maintain the head perpendicular and mid-line without descending through the examiner's hands. On horizontal suspension, the infant should maintain a straight back with the head upright and extremities in flexion position. In comparison, hypotone infants may wrap over the examiner's arms (Leyenaar et al., 2005).

2.4 Data Processing

Descriptive statistics were presented via parameters of central tendency and dispersion, followed by K-S tests for distribution normality. Even with existence of a certain frame for inferential statistics, all analyses follow nonparametric rules, due to consistency towards experimental design and results leading to conclusions based on the nature of analysed and hypothesized phenomena.

Spearman Rank Correlations among variables and Mann-Whitney U Test for comparisons of two independent variables were assessed in TIBCO Software Inc., ver 14.0.0.15. Power analyses and sample size calculations were performed via TIBCO Software Inc., ver 14.0.0.15., and G*Power version 3.1.9.6. Univeresity Kiel, Germany.

2.5 Ethical Issues

Research was approved by Ethical Committee of University Hospital Centre "Sestre milosrdnice"; Vinogradska cesta 29, 10000 Zagreb, Croatia, ICH GCP and Helsinki Declaration; C: 003 06/22-03/003; No: 251-29-11-22-01-7.

3 RESULTS

Table 1 Descriptive statistics and normality distribution test (in Appendices).

Table 2 Spearman Rank Order Correlations (in Appendices).

In addition to basic information about BW and BL, GA at birth for processing the general health of infants, obstetric mode (spontaneous, CS), jaundice (has/none), Apgar score (Casey et al., 2001), which represents the 10-point score has been used to assess the condition and prognosis of new-borns worldwide for the past 70 years, succession of previous pregnancies and born children, etc. are also registered.

Table 3 Descriptive statistics analysis according to obstetric mode of delivery and jaundice (in Appendices).

The obstetric mode of delivery as a previous decision of the physician, and manifested neonatal jaundice as a subsequently established condition, show different statistical strength for distinguishing infants by the results of the measured BW and BL, GA and therefore have impact on decision concerning

age at which the infant should be included in habilitation treatment.

Different disorders from normal tone pattern are shown through results in the observed variables in the Table 3.

Table 4 Descriptive statistical analysis according to muscle tone (in Appendices).

According to the average AFE (Mean±SD:158,36±110,91 for the whole sample, Mean±SD:151,34±127,59 for normal tone) within hypertonic infants a deviation is presented (Mean±SD: 115,67±51,86), which cumulatively with GA (Mean±SD:387,275±55,3798) presents valid information to be furtherly analysed.

Table 5 Mann-Whitney U Test by variable obstetric mode of delivery (in Appendices).

Table 6 Mann-Whitney U Test by variable jaundice (in Appendices).

Table 8 Mann-Whitney U Test by variable muscle tone (between groups 1 and 3) (in Appendices).

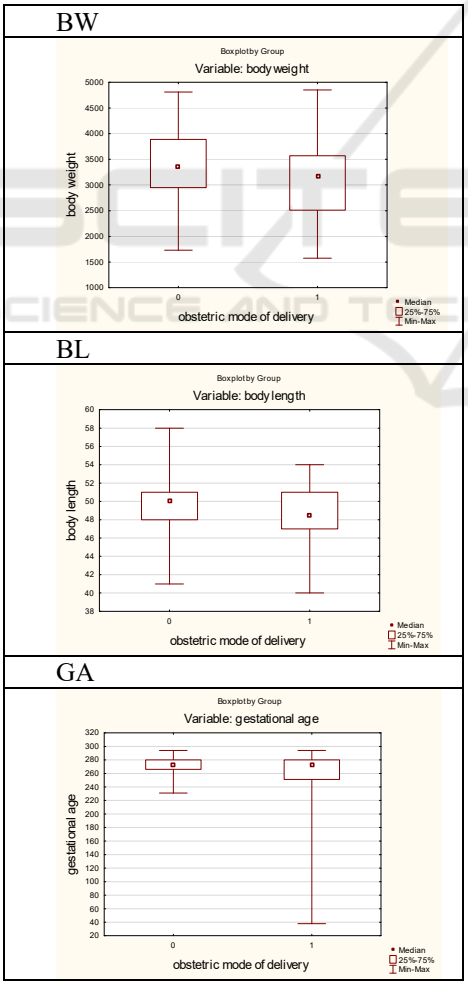

Figure 1: Boxplot by Group (obstetric mode of delivery).

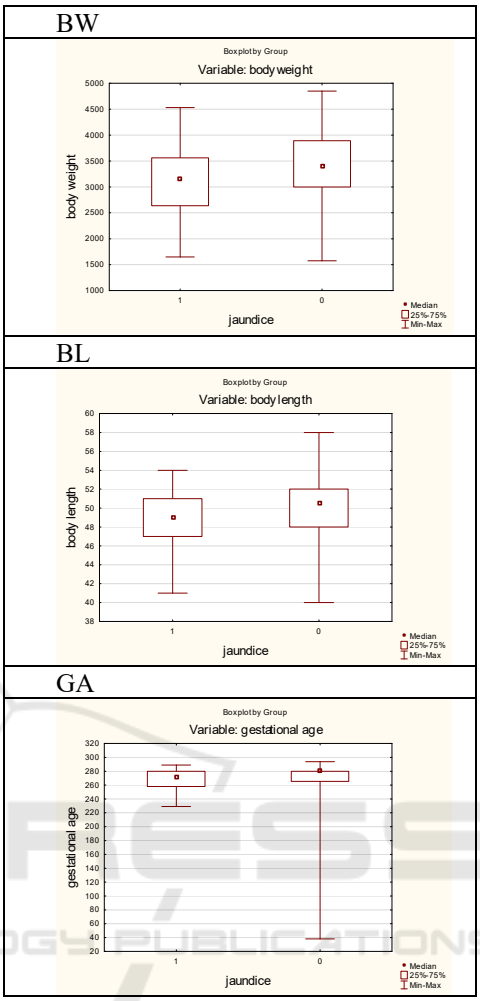

Figure 2: Boxplot by Group (jaundice).

Within series of Mann-Whitney U Tests by variable tone, among all groups 0-3 (0: hypo-, 1:hyper-, 2:normal-; 3:changing), relevant findings are presented in table 7 and graph 3 (between groups 0 and 1), and Table 8 and Graph 4 (between groups 1 and 3).

Table 7 Mann-Whitney U Test by variable muscle tone (between groups 0 and 1) (in Appendices).

4 DISCUSSION AND CONCLUSIONS

Infants with hypotonia, hypertonia and changing muscle tone are frequently associated with adjuvant issues concerning developmental milestones and they pose challenges for clinicians because they may appear be the contributing sign of both benign and serious conditions.

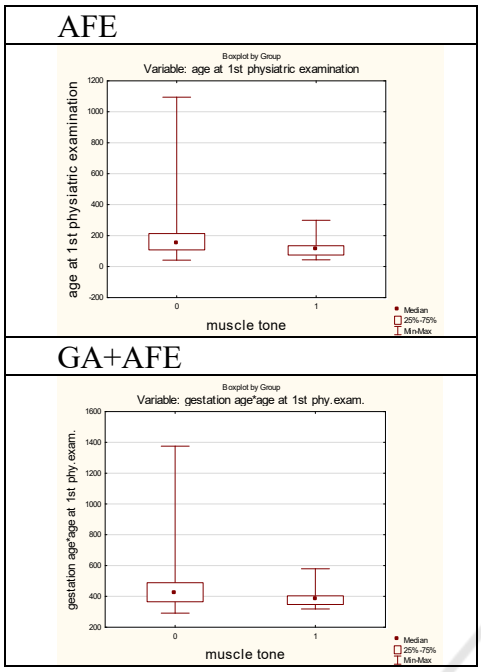

Figure 3: Boxplot by Group (muscle tone).

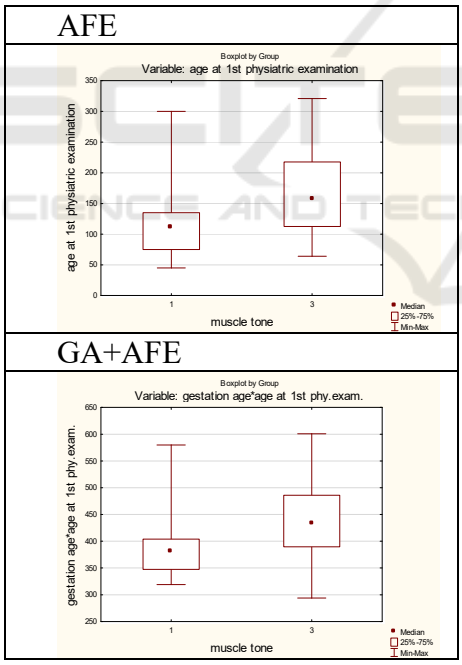

Figure 4: Boxplot by Group (muscle tone).

At first glance, the magnitude of the differential diagnosis, the oddness of associated disturbances, and the ongoing advances in diagnostic interpretation and management may appear overwhelming (Leyenaar et al., 2005). In prospective observational study infants born by prelabour CS were compared with a group of spontaneously born infants. Follow-up assessments were performed at four and twelve months. Prelabour CS (n = 66) had significantly lower results in „Ages and Stages Questionnaire"; adverse neurodevelopmental outcomes in infants born by prelabour CS may be apparent already a few months after birth (Zaigham et al., 2020). Taiwan Birth Cohort Study was designed to assess the developmental trajectories of 24 200 infants born in 2005. Their results implied that the association between CS birth and infant's neurodevelopmental disorders was significantly influenced by GA. Infants born by CS had significant increases in neurodevelopmental disorders (20% compared with infants born by spontaneous delivery) (Chen et al., 2017). In this Swedish population-based birth cohort study of more 1.1 million infants, births via planned or intrapartum CS were associated with a moderately increased risk of neurodevelopmental disorders in infants, but these associations were attenuated after adjusting for familial factors (Zhang et al., 2021). In the representative sample of 4621 singleton infants the objective of analyses was to determine whether there are independent effects of BW and GA on motor and social development (MSD) and the magnitude of effects. Low BW status and preterm delivery are associated independently with small, but measurable, delays in MSD through early childhood and should be considered along with other known risk factors for development delays in determining the need for developmental evaluation (Hediger et al., 2002). In Irish study within the national sample represented of 73,662, infants born by elective or emergency CS may face a delay in cognitive and motor development at age of nine months (Khalaf et al., 2015). In a systematic review there were 28 studies of small for gestational (SGA), with a total of 7861 SGA and 91 619 control appropriate for gestational age (AGA) babies, and three studies of fetal grow restriction (FGR), with a total of 119 FGR and 49 control AGA babies. The findings of the study demonstrate that among infants born at term, being SGA is associated with lower scores on neurodevelopmental outcomes compared to AGA controls (Arcangeli et al., 2012). Developmental changes in the immature central nervous system have a large impact on the expression of atypical motor development. It may happen that a lesion of the developing brain results in neuromotor dysfunction in infancy but is followed by a typical developmental outcome. The reverse may also occur e.g., an apparently typical development in the early phases of infancy may be followed by the development of worst neurodevelopmental outcome-cerebral paralysis (Hadders-Algra, 2004). In infancy,

atypical motor development may be conveyed by a delay in the acquiring of developmental milestones (which may be associated to impaired selection of neurons), by mild, moderate or severe alteration in muscle tone (velocity-dependent resistance to stretch), by a persistence of infantile reflexes (e.g., the Moro or Galant reflex), and by a reduced variation in motor repertoire. The following manifestation may be the most explicit expression of an early lesion of the brain (Hadders-Algra, 2000), (Prechtl, 2001) whereas the other signs may be the outcome of a lesion of the brain but also may be complementary to other types of adversities during early phase of development, such as low-risk preterm delivery (Kostović & Judaš, 2007). Results of this study go in line with previous findings regarding differences in BM ($p<0,01$), BL ($p<0,02$), and GA ($p<0,01$), for CS vs spontaneously born infants (Table 5).

Neurodevelopmental maturation may be impacted by the ability of bilirubin to promote alterations in synaptogenesis, neuritogenesis, and neurogenesis, notably in the premature infant. These clinical manifestations are characterized by the following domains: neuromotor implications; muscle tone abnormalities; hyperexcitable neonatal reflexes; variety of neurobehavior manifestations, expression and language articulation irregularities; and evolving cluster of central processing abnormalities, such as sensorineural, hearing, and visuomotor dysfunctions (Bhutani & Johnson-Hamerman, 2015). In the study among two groups of 20 infants' moderate jaundice is clearly associated with an increase in minor neurologic disorder throughout the infancy in terms of mild irregularities in muscle tone in combination with indicative postural and reflex dysfunction at the age of one year (Soorani-Lunsing et al., n.d.). Thirty-nine term infants with moderate jaundice shortly after delivery, were assessed and compared to 36 infants born at term who did not develop neonatal jaundice. The results of this prospective study demonstrate no significant differences in neurodevelopmental outcome parameters with respect to moderate jaundice between the study groups at age of 3. (Heimler & Sasidharan, 2010). The Dutch study which enrolled 43 healthy term infants showed that up to 18 months of age, term infants with moderate degrees of hyperbilirubinemia have rates of minor neurologic dysfunction similar to those of comparison infants. (Soorani-Lunsing et al., n.d.). The findings of I Soorani-Lunsing et al., study, which used sensitive measures for neurodevelopmental outcome, are in line with the results of three previous studies among 41324 singleton infants that indicated that moderate jaundice (bilirubin<342 μmol/l) in healthy term infants does not affect subsequent neuromotor outcome (Newman & Klebanoff, 1993). The subtler symptoms of bilirubin-induced neurodevelopmental dysfunction (BIND) may be under-recognized and contribute to increased risk of motor impairment such as developmental coordination disorder and learning disabilities (Johnson & Bhutani, 2011). It has been assumed that preterm infants may be more predisposed to develop hearing impairments, whereas on the other hand term infants may more recurrently develop cerebral palsy with associated motor disorders and cerebellar impairment, due to the timing of the bilirubin toxicity in relation to the developing brain area (Shapiro, 2003). Mild kernicterus may manifest with motor symptoms including dystonia with or without athetosis and mild gross motor delays such as late developmental milestones such as age of initiation of walking. These infants generally can ambulate well on their own later in childhood and can speak with some clarity. Infants exposed to lower TB levels, not severe enough to cause kernicterus, may have mild damage to the basal ganglia and cerebellum that may manifest as mild hypotonia, lack of coordination, or generalized clumsiness – not severe enough to be classified as a specific movement disorder (Rose & Vassar, 2015). However, the influence of exposure to low-moderate levels of total bilirubin on the developing CNS is not well understood. Further analysis is needed to identify the range of motor impairments that may result from neonatal jaundice, to perceive the interplay between perinatal risk factors and bilirubin toxicity, and to develop enhanced neuroprotective treatment for motor disorders related to jaundice (Bhutani & Johnson-Hamerman, 2015). Numerous retrospective studies have tried to support or refute the relationship of neonatal jaundice with neurodevelopmental outcomes. A specific objective in understanding this correlation has been the use of differing measures of neurodevelopment. Although neonatal jaundice is quite common, affecting 60%-80% of new-borns overall (Chou et al., 2003), observational data have implicated neonatal jaundice with an elevated risk of later NDI, though these findings have not always been reproduced in following studies (Wusthoff & Loe, 2015).

Results of this study also go in line with previous findings regarding jaundice (Table 6) and differences in BM ($p<0,01$), BL ($p<0,01$), and, with limited statistical power, in GA ($p=0,00$).

Within current research, transversal contextual insights are also necessary to empower understandings of the main findings. E.g. when analysing the

succession of the child in a family (especially between second and forth) statistically significant differences for BW p<0,01, BL p<0,01 and AFE p<0,02 may be pointed out, as well with regard to succession of pregnancy (first and second) for BW p<0,001, BL p<0,001, and with limited statistical power to GA p<0,022). In line with statistically significant differences in chrono-biological variables depending upon the different obstetric modes of delivery (Table 5, Graph 1), as well upon neonatal jaundice (Table 6, Graph 2) importance of correlations among chrono-biological variables is also introduced (Table 2) - statistically significant for BW, BL&GA: 0,62-0,88). When broadened with and compared to infant's AFE, individually and combined with GA (Table 2), correlation matrix (SB: 0,15-0,95) implies the importance of further inter-parametrical insights – in this case with relation to muscle tone classified in 4 groups (normal-, hypo-, hyper-, and changing-).

The most relevant information for the understanding goal of this research regarding representative sample is that - infants with diagnosed increased muscle tone appear to be much earlier referred from primary care to a physiatrist (AS±SD:115,68±51,86 days, in Table 4, compared to average total AS±SD:158,36±110,91 days, in Table 1). The main findings confirm statistically significant differences between infants differently categorized by muscle tone and infant's AFE - among hypertonic and hypotonic (AFE: p=0,00; GA+ AFE: p<0,01; Table 7; Graph 3) as well among hypertonic and changing tone respectively (AFE: p=0,00; GA+ AFE: p<0,01; Table 8; Graph 4).

Conclusively - although there are no correlations between the AFE of the infant with BW, BL (and with GA they are very little correlated - 0.19; Table 2), based on previously presented and discussed findings, it seems that there is a quantitative and measurable indication that the existing categorization by muscle tone indicates the need for more frequent or earlier short 'screening'. It should be embedded into existing official protocols and communication by which it is possible to intervene early enough towards a balanced overall health of the infant.

The main limitation of the study is not predominantly within a variability of clinical practices, but due to different patterns of reference of infants with diagnosed increased muscle tone - from primary care to a physiatrist. Also, future studies must be adequately powered to examine neurodevelopmental impairments due to immature brain lesion among preterm infants separately from term infants. The next step within neurodevelopmental disorders would be stratification obstetric mode of delivery in terms of spontaneous or instrumental vaginal delivery, elective or urgent caesarean section and accompanying severity of manifested neonatal jaundice.

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APPENDIX

Table 1: Descriptive statistics and normality distribution test.

All (N=179)	Mean±SD	Minimum	Maximum	Skewness	Kurtosis	Normality
BW	3267,77±708,69	1575,00	4850,00	-0,16	-0,31	K-S d=0,06, p> 0.20;
BL	49,33±3,09	40,00	58,00	-0,38	0,50	K-S d=0,13, p<0,01
GA	268,46±23,05	38,00	294,00	-5,84	55,57	K-S d=0,17, p<0,01
GA+ AFE	426,83±114,58	256,00	1375,00	3,73	26,22	K-S d=0,15, p<0,01
AFE	158,36±110,91	18,00	1095,00	3,94	28,49	K-S d=0,16, p<0,01

Table 2: Spearman Rank Order Correlations.

	BW	BL	GA	AFE	GA+AFE
BW	1,00	0,87*	0,67*	0,04	0,19*
BL	0,87*	1,00	0,61*	0,02	0,15*
GA	0,67*	0,61*	1,00	0,18	0,39*
AFE	0,04	0,02	0,18*	1,00	0,95*
GA +AFE	0,19*	0,15*	0,39*	0,95*	1,00

*Marked correlations are significant at p <,05.

Table 3: Descriptive statistics analysis according to obstetric mode of delivery and jaundice.

Mean±SD	0(spontaneous): (n=113)	1(CS): (n=66)	0(no jaundice): (n=92	1(jaundice): (n=87)
BW	3381,48±670,93*	3073,09±734,01*	3409,39±713,59*	3118,02±675,69*
BL	49,75±3,031	48,61±3,07*	49,89±3,29	48,74±2,75
GA	272,03±13,92	262,38±32,57	270,50±28,28	266,32±15,62
GA+ AFE	428,58±124,58	423,83±95,92*	428,39±127,82	425,18±99,42
AFE	156,56±122,32	161,45±88,84	157,89±125,11	158,86±94,33

*Normally distributed results K-S test: d, for p> .20.

Table 4: Descriptive statistical analysis according to muscle tone.

Mean±SD	0:hypo (n=88)	1:hyper (n=40)	2:normal (n=23)	3:changing (n=28)
BW	3248,52±694,44*	3297,70±741,39*	3398,57±831,78*	3178,12±611,63*
BL	49,28±3,22	49,20±3,12	49,96±3,23	49,14±2,52*
GA	266,47±29,09	271,60±14,94	271,00±16,74	268,21±13,81
GA + AFE	442,89±133,53	387,28±55,38*	422,35±135,14*	436,57±80,76*
AFE	176,42±129,90	115,68±51,86*	151,35±127,59*	168,36±75,28*

*Normally distributed results K-S test: d, for p> .20.

Table 5: Mann-Whitney U Test by variable obstetric mode of delivery.

	Rank Sum Group 1	Rank Sum Group 2	U	Z	p-value	Z adjusted	p-value	Valid N Group 1	Valid N Group 2
BW	11056,00	5054,00	2843,00	2,64	0,01	2,65	0,01	113	66
BL	10931,50	5178,00	2967,50	2,26	0,02	2,29	0,02	113	66
GA	10987,50	5122,50	2911,50	2,44	0,01	2,48	0,01	113	66
*AFE	9874,50	6235,50	3433,50	-0,88	0,37	-0,88	0,38	113	66
*GA+AFE	10164,50	5945,00	3723,50	-0,01	0,99	-0,014	0,99	113	66

*Interpretations are limited due to results of power/sample size analyses/calculations.

Table 6: Mann-Whitney U Test by variable jaundice.

	Rank Sum Group 1	Rank Sum Group 2	U	Z	p-value	Z adjusted	p-value	Valid N Group 1	Valid N Group 2
BW	6896,00	9214,00	3068,00	-2,69	0,01	-2,69	0,01	87	92
BL	6854,50	9255,50	3026,50	-2,81	0,01	-2,83	0,01	87	92
GA	6769,50	9340,50	2941,50	-3,06	0,00	-3,10	0,00	87	92
*AFE	7885,00	8225,00	3947,00	0,16	0,88	0,16	0,87	87	92
*GA+AFE	7722,500	8387,50	3894,50	-0,31	0,76	-0,31	0,76	87	92

*Interpretations are limited due to results of power/sample size analyses/calculations.

Table 7: Mann-Whitney U Test by variable muscle tone (between groups 0 and 1).

	Rank Sum Group 1	Rank Sum Group 2	U	Z	p-value	Z adjusted	p-value	Valid N Group 1	Valid N Group 2	2*1sided exact p
AFE	6329,50	1926,50	1106,50	3,36	0,00	3,36	0,00	88	40	0,00
GA+ AFE	6213,00	2043,00	1223,00	2,76	0,01	2,76	0,01	88	40	0,01

Table 8: Mann-Whitney U Test by variable muscle tone (between groups 1 and 3).

	Rank Sum Group 1	Rank Sum Group 2	U	Z	p-value	Z adjusted	p-value	Valid N Group 1	Valid N Group 2	2*1sided exact p
AFE	1128,00	1218,00	308,00	-3,13	0,00	-3,14	0,00	40	28	0,00
GA+AFE	1158,00	1188,00	338,00	-2,76	0,01	-2,76	0,01	40	28	0,01