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Assessment of general movements and heart rate variability in prediction of neurodevelopmental outcome in preterm infants

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ABSTRACT

Background: Adverse neurologic outcome in preterm infants could be associated with abnormal heart rate (HR) characteristics as well as with abnormal general movements (GMs) in the 1st month of life.
Aims: To demonstrate to what extent GMs assessment can predict neurological outcome in preterm infants in our clinical setting; and to assess the clinical usefulness of time-domain indices of heart rate variability (HRV) in improving predictive value of poor repertoire (PR) GMs in writhing period.
Study design: Qualitative assessment of GMs at 1 and 3 months corrected age; 24 h electrocardiography (ECG) recordings and analyzing HRV at 1 month corrected age.
Subjects: Seventy nine premature infants at risk of neurodevelopmental impairments were included prospectively.
Outcome measures: Neurodevelopmental outcome was assessed at the age of 2 years corrected. Children were classified as having normal neurodevelopmental status, minor neurologic dysfunction (MND), or cerebral palsy (CP).
Results: We found that GMs in writhing period (1 month corrected age) predicted CP at 2 years with sensitivity of 100%, and specificity of 72.1%. Our results demonstrated the excellent predictive value of cramped synchronized (CS) GMs, but not of PR pattern. Analyzing separately a group of infants with PR GMs we found significantly lower values of HRV parameters in infants who later developed CP or MND vs. infants with PR GMs who had normal outcome.
Conclusions: The quality of GMs was predictive for neurodevelopmental outcome at 2 years. Prediction of PR GMs was significantly enhanced with analyzing HRV parameters.

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1. Introduction

In recent decades, major advances in neonatal medicine have led to the increase of survival rates of preterm-born infants [1]. With survival rates of preterm and/or low-birth weight infants improving, there is an increase in the number of these infants developing motor, sensory, cognitive, and many other neurodevelopmental problems later in life. Motor problems can range from developmental coordination disorders to cerebral palsy (CP) [2]. Consequently, it is of paramount importance to identify motor dysfunction in infants at an early stage so that appropriate interventions can be implemented [2,3].

There are a number of assessments that enable the motor development of preterm infants during the first year of life to be discriminated, predicted and evaluated. At present, it is estimated that Prechtl's method on the qualitative assessment of general movements (GMs) is one of the best methods for evaluating neurologic function in young infants and has a high predictive value for future neurologic deficits [4–7]. GMs as complex, endogenously generated movements involving the whole body are present from early foetal life until the end of the second month after term. Throughout this period, general movements have a writhing character: they are ellipsoid and create the impression

Abbreviations: GMs, general movements; HR, heart rate; HRV, heart rate variability; MND, minor neurologic dysfunction; CP, cerebral palsy; NN intervals, the length between two successive heart beats; SDNN, standard deviation of all NN intervals; SDANN, standard deviation of the averages of NN intervals in all five-minute segments; RMSSD, square root of the mean of the sum of the squares of the differences between adjacent NN intervals.

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that the infant is writhing. Usually 2 months after term the writhing GMs are gradually replaced by fidgety GMs. The characteristics of fidgety movements are: small amplitude, moderate speed, and variable acceleration of the neck, trunk and limbs in all directions. These movements are present up to 5 months after term [8,9].

GMs in the writhing period in at-risk and brain-damaged infants lose their complex and variable character and have either a poor repertoire (PR) or are cramped-synchronized (CS) or chaotic (Ch). Fidgety movements can be either abnormal or absent.

In the writhing period it is only the abnormal pattern of CS GMs that has a high predictive value for later spastic CP. The abnormal pattern of PR GMs is frequent in preterm infants, but has a low predictive value, so it is highly recommended to assess fidgety movements in these infants. It is only the presence or absence of fidgety movements that has a high predictive value for the neurological outcome [10–12].

Investigations regarding CP and neurodevelopmental disturbances are focused on central nervous system (CNS) damage, while studies of the function of the autonomic nervous system (ANS) have been virtually overlooked. There are a small number of studies describing heart autonomic irregularity among children with CP [13–14].

The ANS is a crucial regulator of the homeostasis of the circulatory and respiratory system. Parasympathetic and sympathetic controls of heart rate (HR) constantly mature with gestational age. After birth, there is a progressive HR decrease and heart rate variability (HRV) indices increase. Maturation of the ANS, on the one hand, allows the full-term newborn to adapt its respiratory and haemodynamic responses to internal and external environments. The premature newborn, on the other hand, may inappropriately adapt to environmental, nutritional or iatrogenic external conditions due to ANS immaturity. There is significantly lower ANS activity in premature than in term infants [15].

HR and HRV are powerful tools that allow not only the cardiovascular system but also the CNS to be studied. One of the clinical applications of HRV measurements in preterm infants is the prediction of neurological outcome [16].

In our previous study, we demonstrated that HRV could be helpful clinically as well as a prognostic tool in infants with developmental coordination disorders. This study was the first to report the relationship between 24 h HRV time-domain indices and the infant neurodevelopmental status as well as their neurodevelopmental outcome, favouring a hypothesis of enhanced sympathetic and low parasympathetic nervous system activity in infants with neurodevelopmental abnormalities [17,18].

The purpose of the current study was to demonstrate the extent to which GM assessment can predict neurological outcome in preterm infants in our clinical setting; and to assess the clinical usefulness of time-domain indices of HRV in improving the predictive value of PR GMs in the writhing period.

2. Methods

We collected the consecutive sample of 94 children, born at a gestational age of below 37 weeks, admitted at the tertiary referred Paediatric Rehabilitation Department of the University Hospital from July 2011 to December 2013. The reasons for admission were a high risk of neurodevelopmental problems or abnormal findings in paediatric examinations (such as hypotonia, hypertonia, abnormal reflexes, abnormal postural responses, abnormal posture, asymmetry, abnormal findings of cranial ultrasound etc.). At the admission to our institution all children were near the term age (37–41 weeks post-menstrual age (PMA)).

During the study 15 children were excluded due to: presence of congenital anomalies – 4; incorrect video recording of GMs – 2; incorrect ECG – 1; lost to follow-up – 7; and one child died. Finally, 79 children were included in the study. The study was performed in accordance with the Declaration of Helsinki and under the principles of Good Clinical Practice. The local ethic board approved the study and written informed consent was obtained from the parents or caregivers of each infant. The protocol consisted of the following assessments: a) video recordings and evaluation of GMs, b) 24 h ECG Holter monitoring and HRV analyses, c) neurological examination.

a) Video recordings and evaluation of GMs. Two digital video recordings were made of each infant: at 1 month corrected age, for assessment of writhing movements, and the second at 3 months after term, the age at which fidgety movements should be present. During recordings, the infant was lying on an uncoloured underlay, in the supine position, wearing only a nappy with their face clearly visible. The duration of the recording was at least 10 min with the infant in adequate behavioural state 4 (eyes open, not crying, irregular respiration, movements present). The recordings were evaluated by the observer, who had successfully participated in both a basic and an advanced GM training course. She had several years of experience in rating children by Prechtl's method in clinical practice. For this study she was blind to clinical history details, and she used the same standardized rating sheet that was used during the training courses with indications of the age of the child, the case number and the different rating possibilities:
For writhing period: N = normal writhing GMs (the movements are complex, variable, fluent, elegant, the entire body involved, with variable sequences of the arms, legs, neck and trunk); PR = poor repertoire GMs (the sequence of the successive movement components is monotonous and the movements of the different body parts do not occur in the normal rich and complex sequence); Ch = chaotic GMs (movements of all limbs are of large amplitude and occur in a chaotic order without any fluency or smoothness, and consistently appear to be abrupt); CS = cramped-synchronized GMs (movements appear stiff and rigid, without normal smooth and fluent character, all limb and trunk muscles contract and relax almost simultaneously).
For fidgety period: F = normal fidgety GMs (elegant movements of small amplitude, moderate speed, and variable acceleration of the neck, trunk and limbs in all directions, present continually or intermittently in the awake infant); AF = abnormal fidgety GMs (excessive amplitude, speed and jerkiness); and F− = absent fidgety GMs (no fidgety movements).
b) 24 h ECG Holter monitoring and HRV analyses. 24 h ECG–Holter monitoring was performed by small, ambulatory, portable device (Cardiolight FMC.A, Medset and Medizintechnik, Hamburg, Germany) at the age of 1 month after term. To determine HRV parameters, appropriate Holter software was used. Before HRV analyses we checked the precision of computer-assisted methods, and whether premature QRS complexes were excluded from HRV software analyses. The method of QRS detection was than overread by a physician, and all remaining ectopic beats, noisy data and artefacts were manually identified, and thus excluded from the HRV analysis. Only the normal NN intervals (the length between two successive heart beats) over a period of at least 18 h of analysable signal were analysed using the time-domain method. Observed time-domain parameters included: standard deviation of all NN intervals (SDNN), standard deviation of the averages of NN intervals in all 5-min segments (SDANN), and the square root of the mean of the sum of the squares of the differences between adjacent NN intervals (RMSSD). An HRV analysis was performed by one of the authors who was unaware of infants' neurological findings.
c) Neurological examination. At age 24 months corrected, a structured neurological examination was performed by a neurologist employed at the Paediatric neurology Department, well experienced and educated in the field of child neurology, for assessment of posture, reflexes, muscular tone and movements. The neurologic status was categorized as: Normal (completely normal neurologic status); Unspecific signs or MND (minor neurologic dysfunction) according to Touwen's criteria [19,20], but no definite signs of CP; and CP

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