Early Human Development 141 (2020) 104935

Contents lists available at ScienceDirect

Early Human Development

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

Early preterm infants with abnormal psychomotor neurodevelopmental outcome at age two show alterations in amplitude-integrated electroencephalography signals

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ARTICLE INFO

Keywords:
Amplitude-integrated electroencephalography
Burdjalov score
Neurodevelopmental outcome
Preterm infant

ABSTRACT

Introduction: Recent studies showed that neurodevelopment in preterm infants can be predicted by using amplitude-integrated electroencephalography (aEEG)-derived parameters. In our previous study we demonstrated that aEEG could be useful in predicting neurodevelopmental outcome in very preterm infants at the corrected age of 2 years.

Aim: The aim of this study was to further evaluate aEEG for predicting neurodevelopmental outcome at the at the corrected age of 2 years in preterm infants.

Methods: Between July 2010 and June 2016 440 very preterm infants were eligible for the study at Innsbruck Medical University Hospital. The aEEG was evaluated for the Burdjalov score in 306 preterm infants (mean gestational age 29.5 weeks; range: 24.1–31.9 weeks). At the corrected age of 2 years outcome was assessed by the Bayley Scales of Infant and Toddler Development.

Results: The cohort was divided into three subgroups: 248 infants with normal outcome, 40 infants with delayed outcome and 18 infants with abnormal outcome. Burdjalov scores were lower in infants with delayed outcome than in infants with normal outcome and even lower in infants with abnormal outcome. Post-hoc analysis showed significant differences between normal and delayed psychomotor outcome at 18–24 h (5 (3;6) versus 3 (3;5), $p = .024$), 30–36 h (6 (4;8) versus 4 (4;6), $p = .033$), 42–48 h (7 (5;8.5) versus 4 (4;7), $p = .003$), 54–60 h (7 (6;9) versus 5 (4;7), $p = .003$), 66–72 h (8 (6;9) versus 6.5 (4.25;7.75), $p = .027$) and week one (8 (7;10) versus 6.5 (5;8), $p = .021$). Additionally, when comparing normal to abnormal outcome, a significant difference was found at week four (12 (9;12) versus 8 (7;10), $p = .024$). The Burdjalov score was only predictive for a delayed psychomotor outcome, presenting the highest area under the curve (0.690) at week two of life.

Conclusion: We observed differences in aEEG signals and neurodevelopmental outcome at the corrected age of 2 years, especially for psychomotor outcome. The predictive value of the Burdjalov score regarding neurodevelopmental outcome at the corrected age of 2 years in preterm infants was low.

1. Introduction

About 15 million babies are born before 37 weeks gestational age (preterm) worldwide every year. Mortality in preterm infants has been significantly reduced due to progress in obstetrical and neonatal care. However, morbidity is still of great concern, because preterm infants frequently display neurological sequelae including disturbances in cerebral grey and white matter brain development [1]. In long-term preterm infants suffer from psychomotor and cognitive difficulties, which could be improved by identifying infants at high risk and offering special care and extra resources, such as physical therapy, speech and occupational therapy, and different sorts of education services. The evaluation of brain function complements neurological diagnostic methods used to provide important information in order to identify infants at risk and to offer best care to the preterm infant, to advice and to support the parents and caregivers [2]. Associations of amplitude-integrated electroencephalography (aEEG)-derived parameters with short-term adverse outcome, such as intracerebral haemorrhage or death, have been reported in preterm infants [3]. Changes in aEEG signals associated with long-term development have been indicated

*Abbreviations:*aEEG, Amplitude-integrated electroencephalography

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https://doi.org/10.1016/j.earlhumdev.2019.104935
Received 5 August 2019; Received in revised form 26 November 2019; Accepted 2 December 2019

[4,5]. Klebermass et al. reported that one aEEG recorded within the first 2 weeks of life predicts outcome at the age of three in preterm infants born < 30 weeks gestational age [6]. Song et al. showed that severely abnormal aEEG recordings within 72 h of life can predict brain injury and poor outcome at 18 months of age [7]. Wikström et al. showed that neurodevelopmental outcome at the age of two can be predicted by aEEG on the first day of life [8]. In contrast El Ters et al. showed that aEEG at term equivalent age correlated with delayed development at 24 to 36 months of age [9]. In a recent meta-analysis including three studies Fogtmann et al. concluded that aEEG might be useful to predict neurodevelopmental outcome in preterm infants, however, due to high risk of bias, further studies are needed [10].

By performing standardised scheduled aEEG recordings in the first 4 weeks of life we found in our previous study, that the predictive value of aEEG for neurodevelopmental outcome of preterm infants at the age of 1 year was highest within the first 36 h of life [11]. The aim of this study was to further evaluate whether aEEG in preterm infants is useful in predicting neurodevelopmental outcome at the age of 2 years.

2. Methods

The study survey area was Tyrol, a state in western Austria with 680,000 inhabitants and about 7000 live births per year. Infants born before 32 completed weeks of pregnancy at Innsbruck Medical University Hospital, which is the only neonatal intensive care unit in this geographical region, were enrolled. The study was performed as a retrospective analysis of prospectively collected data. The survey period was July 2010 to June 2016 (440 live births). Twenty-three infants were diagnosed with major congenital anomalies or congenital infection. Eight infants died. In 13 infants no aEEG recording could be obtained due to personnel (no person trained in aEEG application available) or technical reasons (aEEG monitor broken, no electrodes available). Thirty-four infants moved out of the region or were non-residents. Thus, 362 children were invited for a detailed follow-up visit at a corrected age of 2 years. A total of 32 (8.1%) parents did not accept the invitation and 24 infants (6.1%) were non-compliant. As a result, 306 children formed the current study population (Fig. 1). The study was approved by the Ethics Committee of the Medical University of Innsbruck (Study No. AN2013-0086 333/4.2). Maternal and neonatal data were collected during hospital stay as described in our previous papers [12,13]. Maternal and neonatal data of the study cohort are shown in Table 1. Growth charts developed by Fenton et al. were used to classify infants as small for gestational age at birth, defined as a birth weight below the 10th percentile for sex and gestational age [14].

2.1. aEEG recording and assessment

Two-channel aEEG was recorded with the BrainZ instruments BRM3 monitor (Natus Medical Inc., San Carlos, CA, USA) from adhesive electrodes and assessed according to Burdjalov et al. as described in our previous paper [12,15]. aEEG recordings were conducted in a standardised schedule during the first 72 h of life and then at week one, two, three and four. Recordings were assessed on 10 defined time points (6–12 h, 18–24 h, 30–36 h, 42–48 h, 54–60 h, 66–72 h, week one, week two, week three and week four).

2.2. Neurodevelopmental outcome

Neurodevelopmental outcome was assessed at the age of two by neurological examinations and the Bayley Scales of Infant and Toddler Development, second edition (Bayley-II) [16] for infants born between 2007 and 2013 and third edition (Bayley III) [17] for infants born between 2014 and 2016. For Bayley-III German norms were used [18]. Bayley-II scores provide psychomotor and mental developmental indices, Bayley-III scores motor composite, and mental developmental scores (mean of cognitive and language composite scores). The mean score is 100, and a score of < 85 (> 1 standard deviation below the mean) and ≥ 70 (≤2 standard deviations below the mean) indicates a delay and a score of < 70 (> 2 standard deviations below the mean) indicates abnormal development. Delayed neurodevelopmental outcome was defined as a score of < 85 and ≥ 70. Abnormal neurodevelopmental outcome was defined as a score of < 70 on either the psychomotor or mental developmental index of the Bayley-II or the motor composite or mental developmental score of the Bayley-III. For comparison of Bayley-II and Bayley III, a composite score was calculated by average of the Bayley-III cognitive and language scales as described previously [19]. All tests were performed by one of two experienced psychologists.

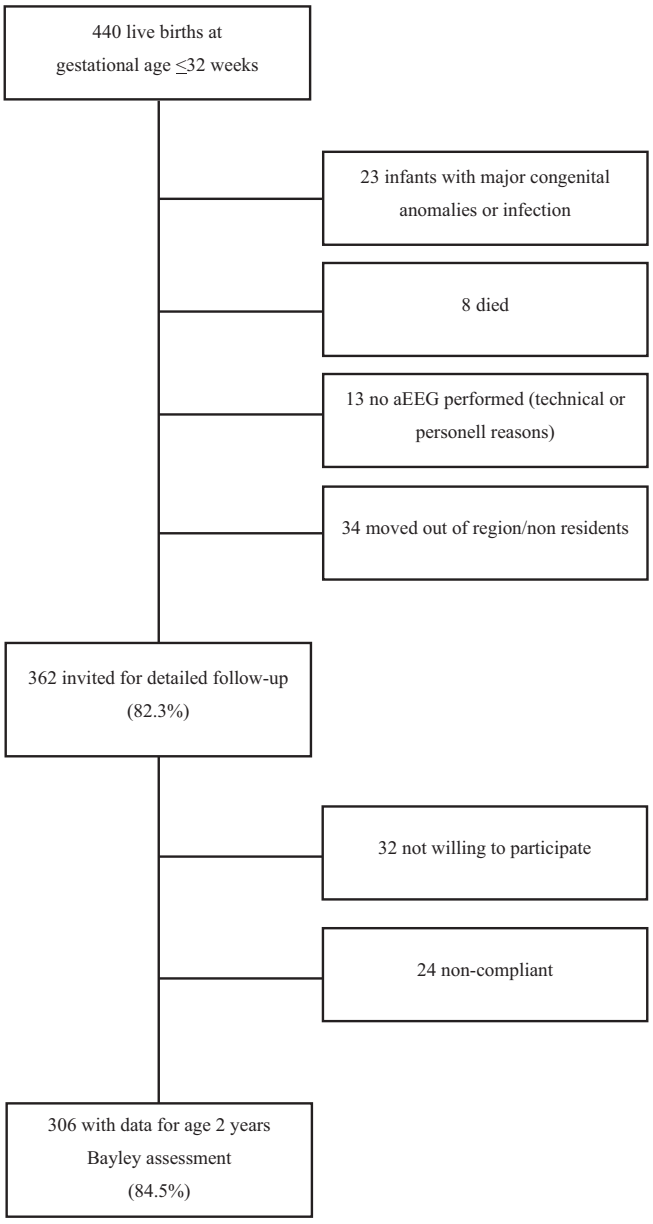

Fig. 1. Flow chart for the inclusion of very preterm infants. Overview of children assessed for eligibility and enrolled in the study. aEEG = amplitude-integrated electroencephalography.

2.3. Clinical variables as potential confounders

We accounted for being born small for gestational age and late-onset sepsis, because these factors are known to influence aEEG and outcomes

Table 1
Sociodemographic and neonatal characteristics.

Variable	Normal outcome $N = 248$	Delayed outcome $N = 40$	Abnormal outcome $N = 18$	p value
Gestational age (weeks) mean (± SD)	29.62 ± 1.93	29.46 ± 2.05	28.70 ± 2.34	0.242
Birthweight (g) mean (± SD)	1299.91 ± 366.16	1167.35 ± 391.05	1237.05 ± 526.36	0.144
Male n (%)	126 (50.8)	20 (50.0)	10 (55.6)	0.919
Maternal age < 23 years n (%)	11 (4.4)	3 (7.5)	1 (5.6)	0.701
Maternal education < 12 years n (%)	85 (34.3)	26 (65.0)	8 (44.4)	**0.034**
Smoking in pregnancy n (%)	25 (10.1)	8 (20.0)	4 (22.2)	0.069
Siblings n (%)	82 (33.1)	14 (35.0)	8 (44.4)	0.608
Premature rupture of membranes n (%)	63 (25.4)	9 (22.5)	4 (22.2)	0.931
Antenatal steroids n (%)	227 (91.5)	36 (90.0)	17 (94.4)	0.897
Small for gestational age n (%)	14 (5.6)	8 (20.0)	2 (11.1)	**0.007**
Bronchopulmonary dysplasia n (%)	50 (20.2)	17 (42.5)	9 (50.0)	**0.001**
Intracerebral haemorrhage III-IV n (%)	9 (3.6)	0 (0.0)	1 (5.6)	0.418
Necrotizing enterocolitis n (%)	7 (2.8)	0 (0.0)	3 (16.7)	**0.003**
Retinopathy of prematurity grade 3–4 n (%)	8 (3.2)	4 (10.0)	1 (5.6)	0.141
Early-onset sepsis n (%)	15 (6.0)	2 (5.0)	1 (5.6)	0.968
Late-onset sepsis n (%)	22 (8.9)	4 (10.0)	5 (27.8)	**0.028**

Study group by outcome with n (%), mean (standard deviation), median (25th and 75th percentile). P values are from the Kruskal-Wallis test. Information on maternal education could not be obtained in 100 (32.7%) subjects. In all other variables the proportion of missing data was < 5%.
The results were deemed statistically significant when the two-sided *p value* was < 0.05 (shown bold in all tables).

[20–22].

2.4. Statistical analysis

The data analysis was performed using SPSS software version 24.0 for Windows (SPSS Inc., Chicago, IL, USA). We used the Kruskal-Wallis test with subsequent nonparametric multiple comparison testing for multiple comparisons. A logistic regression analysis was applied to assess differences between preterm infants with normal and abnormal outcomes and potential confounders. Model A was adjusted for small for gestational age. Model B was adjusted for late-onset sepsis. Model C was adjusted for small for gestational age and late-onset sepsis. Data are presented as numbers with percentages, medians with interquartile ranges or means with standard deviations or 95% confidence intervals. The results were deemed statistically significant when the two-sided *p* value was < 0.05. The receiver operator characteristic and area under the curve were computed to determine cut-off levels and enable us to calculate the sensitivity, specificity, positive predictive value and negative predictive value.

3. Results

3.1. Study participants

In this study 306 preterm infants with a mean gestational age of 29.5 (range 24.1–31.9) weeks and a birth weight of 1.279 (range 400–2180) grams were included. In total 248 infants (81%) were defined as having normal developmental outcome, 40 infants (13.1%) were classified as having delayed outcome and 18 infants (5.9%) as having abnormal outcome. When assessing the psychomotor or mental developmental index separately, 261 infants (85.3%) showed normal psychomotor development, 29 (9.5%) delayed and 11 infants (3.6%) abnormal psychomotor outcome. Analysis of the mental developmental index showed that 255 infants (83.3%) had a normal score, 29 (9.5%) were having delayed and 14 infants (4.6%) abnormal outcome.

3.2. The Burdjalov score was predictive for a delayed psychomotor outcome

The Burdjalov score increased in all three groups with postnatal age and was higher in infants with normal outcome as compared to abnormal outcome (see Table 2). Significant overall differences were detected between the three groups by Kruskal-Wallis analysis at postnatal day two ($p < .05$), but significance was lost after post-hoc analysis. When focusing on psychomotor outcome, we observed that the Burdjalov score increased in all groups with postnatal age. Differences between groups calculated by Kruskal-Wallis analysis were found (see Table 3). Post-hoc analysis showed significant differences between normal and delayed outcome at 18–24 h ($p = .024$), 30–36 h ($p = .033$), 42–48 h ($p = .003$), 54–60 h (p = .003), 66–72 h ($p = .027$) and week one ($p = .021$). Additionally, when comparing normal to abnormal outcome, a significant difference was found at week four (p = .024). Logistic regression analysis showed consistent results after adjusting for late-onset sepsis and being born small for gestational age (Table 4).

When focusing on cognitive development, the Burdjalov score increased in all groups with postnatal age over time. Results are shown in Table 5.Significant differences were found at week 1 and week 2. Post-hoc analysis showed a significant difference between normal outcome and abnormal outcome at 30–36 h ($p = .030$).

Table 2
Burdjalov score and neurodevelopmental outcome at 24 months of corrected age.

	Normal outcome median (IQR)	Delayed outcome median (IQR)	Abnormal outcome median (IQR)	P value
6–12 h	3.00 (2.00;4.00)	3.00 (2.00;4.00)	2.50 (2.00;3.00)	0.406
18–24 h	5.00 (3.00;6.00)	5.00 (3.00;7.00)	4.00 (3.00;5.00)	0.263
30–36 h	6.00 (4.00;8.00)	5.00 (4.00;7.00)	4.50 (4.00;5.75)	0.110
42–48 h	7.00 (5.00;9.00)	5.00 (4.00;7.00)	5.00 (4.00;6.00)	**0.023**
54–60 h	7.00 (5.00;9.00)	7.00 (4.00;8.00)	5.00 (4.00;7.00)	0.058
66–72 h	7.00 (6.00;9.00)	7.00 (5.00;8.75)	5.50 (4.00;7.75)	0.071
Week 1	8.00 (7.00;10.00)	8.00 (5.00;10.00)	6.50 (4.75;9.00)	0.077
Week 2	9.00 (7.00;11.00)	9.00 (7.00;11.00)	7.50 (5.00;9.50)	0.056
Week 3	11.00 (8.00;12.00)	11.00 (8.00;12.00)	8.50 (5.00;12.00)	0.366
Week 4	12.00 (9.00;12.00)	11.00 (8.00;13.00)	9.00 (7,25;11.50)	0.082

Burdjalov score (median, interquartile range (IQR)) at each time point by group. *P* values are from the Kruskal-Wallis test.
The results were deemed statistically significant when the two-sided *p value* was < 0.05 (shown bold in all tables).

Table 3
Burdjalov score and psychomotor developmental outcome at 24 months of corrected age.

	Normal psychomotor outcome median (IQR)	Delayed psychomotor outcome median (IQR)	Abnormal psychomotor outcome median (IQR)	P value
6–12 h	3.00 (2.00;4.00)	3.00 (2.00;3.00)	3.00 (2.00;3.00)	0.510
18–24 h	5.00 (3.00;6.00)	3.00 (3.00;5.00)	4.00 (3.00;5.00)	**0.021**
30–36 h	6.00 (4.00;8.00)	4.00 (4.00;6.00)	5.00 (4.00;8.00)	**0.037**
42–48 h	7.00 (5.00;8.50)	4.00 (4.00;7.00)	4.50 (4.00;6.75)	**0.002**
54–60 h	7.00 (6.00;9.00)	5.00 (4.00;7.00)	5.00 (4.00;8.50)	**0.001**
66–72 h	8.00 (6.00;9.00)	6.50 (4.25;7.75)	5.00 (4.00;9.00)	**0.011**
Week 1	8.00 (7.00;10.00)	6.50 (5.00;8.00)	6.50 (3.75;9.00)	**0.008**
Week 2	9.00 (7.00;11.00)	8.00 (7.00;9.75)	7.00 (5.00;10.00)	**0.025**
Week 3	11.00 (8.00;12.00)	10.00 (8.00;12.00)	8.00 (5.00;10.75)	0.281
Week 4	12.00 (9.00;12.00)	10.00 (8.00;12.00)	8.00 (7.00;10.00)	**0.008**

Burdjalov score (median, interquartile range (IQR)) at each time point by group. P values are from the Kruskal-Wallis test.
The results were deemed statistically significant when the two-sided *p value* was < 0.05 (shown bold in all tables).

Table 4
Logistic regression analysis of Burdjalov scores in preterm infants with normal and abnormal psychomotor developmental outcome.

Outcome variable and analysis	β coefficient	P value	OR (95% CI)
Burdjalov score 18–24 h			
Unadjusted	−0.226	0.030	0.8 (0.6,1.0)
Model A	−0.208	0.053	0.8 (0.6,1.0)
Model B	−0.222	0.040	0.8 (0.6;1.0)
Model C	−0.211	0.058	0.8 (0.6;1.0)
Burdjalov score 30–36 h			
Unadjusted	−0.202	0.024	0.8 (0.7,1.0)
Model A	−0.178	0.057	0.8 (0.7,1.0)
Model B	−0.172	0.070	0.8 (0.7;1.0)
Model C	−0.161	0.101	0.9 (0.7,1.0)
Burdjalov score 42–48 h			
Unadjusted	−0.276	0.002	0.7 (0.6,0.9)
Model A	−0.242	0.009	0.8 (0.6,0.9)
Model B	−0.241	0.010	0.8 (0.6;0.9)
Model C	−0.217	0.025	0.8 (0.7,1.0)
Burdjalov score 54–60 h			
Unadjusted	−0.327	0.001	0.7 (0.6,0.9)
Model A	−0.291	0.003	0.7 (0.6,0.9)
Model B	−0.283	0.004	0.8 (0.6;0.9)
Model C	−0.260	0.012	0.8 (0.6,0.9)
Burdjalov score 66–72 h			
Unadjusted	−0.274	0.003	0.8 (0.6,0.9)
Model A	−0.255	0.009	0.8 (0.6,0.9)
Model B	−0.231	0.018	0.8 (0.7;1.0)
Model C	−0.224	0.030	0.8 (0.7,1.0)
Burdjalov score week 1			
Unadjusted	−0.267	0.002	0.8 (0.6,0.9)
Model A	−0.229	0.011	0.8 (0.7,0.9)
Model B	−0.232	0.010	0.8 (0.7;0.9)
Model C	−0.214	0.023	0.8 (0.7,1.0)

Model A was adjusted for small for gestational age. Model B was adjusted for late-onset sepsis. Model C was adjusted for small for gestational age and late-onset sepsis. Odds ratios (OR) are reported as odds ratio per standard deviation increase with 95% confidence interval (CI).

3.3. The Burdjalov score most accurately predicted psychomotor developmental outcome

Receiver operator characteristic curves were computed for information on the predictive value of the Burdjalov score regarding overall neurodevelopmental outcome at the age of two. Receiver operator characteristic curves showed no predictive value of the Burdjalov score for overall neurodevelopmental outcome (Fig. 2). When separately computing the receiver operator characteristic curves for the psychomotor (Fig. 3) and mental developmental index (Fig. 4), a predictive value for the psychomotor developmental index was observed. The area under the curve showed highest values at week two (0.690). Under the assumption that infants with scores of eight or less at the age of 4 weeks will likely suffer from delay in psychomotor outcome, sensitivity was seen to be 63%, specificity 64%, a positive predictive value 21% and a negative predictive value 92%.

Table 5
Burdjalov score and mental developmental outcome at 24 months of corrected age.

	Normal mental outcome median (IQR)	Delayed mental outcome median (IQR)	Abnormal mental outcome median (IQR)	p value
6–12 h	3.00 (2.00;4.00)	3.00 (2.00;5.00)	2.50 (2.00;3.00)	0.222
18–24 h	5.00 (3.00;6.00)	5.00 (3.00;7.00)	3.50 (3.00;5.00)	**0.022**
30–36 h	6.00 (4.00;8.00)	6.00 (4.00;7.00)	4.00 (4.00;5.00)	**0.035**
42–48 h	7.00 (5.00;8.00)	6.00 (5.00;8.00)	5.00 (4.00;6.25)	0.132
54–60 h	7.00 (5.00;9.00)	7.00 (6.00;8.00)	5.50 (4.25;7.75)	0.131
66–72 h	7.00 (6.00;9.00)	7.00 (6.00;10.00)	7.00 (4.00;8.00)	0.388
Week 1	8.00 (6.00;9.25)	9.00 (6.00;10.00)	7.00 (5.25;9.75)	0.529
Week 2	9.00 (7.00;11.00)	9.00 (8.00;11.00)	8.00 (5.00;10.00)	0.097
Week 3	11.00 (8.00;12.00)	11.00 (8.00;12.00)	9.00 (5.00;12.00)	0.481
Week 4	12.00 (9.00;12.00)	10.00 (9.00;12.50)	10.50 (8.25;12.00)	0.432

Burdjalov score (median, interquartile range (IQR)) at each time point by group. *P* values are from the Kruskal-Wallis test.
The results were deemed statistically significant when the two-sided *p value* was < 0.05 (shown bold in all tables).

4. Discussion

Premature birth poses the infant at risk for structural and functional disturbances of brain development. Prognosis of later outcome is challenging, especially in infants without obvious brain injury. Identification of a biomarker would be of great interest, helping physicians to improve diagnosis and prognosis of preterm infants. The gold standard for imaging the newborn brain is cranial ultrasonography, which is a non-invasive, reliable, safe and radiation-free tool for demonstrating and following brain injury in preterm infants, but with regard to the preterm brain it has its limitations. Nowadays magnetic resonance imaging is additionally used to image the preterm brain, because it gives detailed information about brain development, cortical folding and myelination and superior to ultrasonography it gives the extent and localization of diffuse white matter injury more precisely [23]. In addition to structural evaluation of brain morphology, continuous evaluation of brain function, such as using aEEG, seems to become another important factor in preterm care. A correlation of aEEG parameters with neurodevelopmental outcome in preterm infants has been reported in previous studies [4,5,22]. We observed a maturation of aEEG patterns with increasing postnatal age [24] and a predictive value of the aEEG, when performed in the neonatal period [7,10,25,26]. Despite the numerous numbers of studies that investigated the predictive value of aEEG for neurodevelopmental outcome, data on aEEG recordings performed at a later age and their relevance for outcome prediction are scarce. This might be due to the fact that placement of aEEG electrodes in very preterm infants at a later age is more difficult, more time consuming and due to need of serial electrode sets more expensive. In this study, we further evaluated the aEEG score introduced by Burdjalov et al. in the first 72 h and 4 weeks of life in a cohort of prematurely born infants below 32 weeks gestation with respect to neurodevelopmental outcome at 24 months corrected age. We found no differences in the Burdjalov score regarding overall neurodevelopmental outcome. However, focusing on the psychomotor developmental index we detected differences in the Burdjalov total score

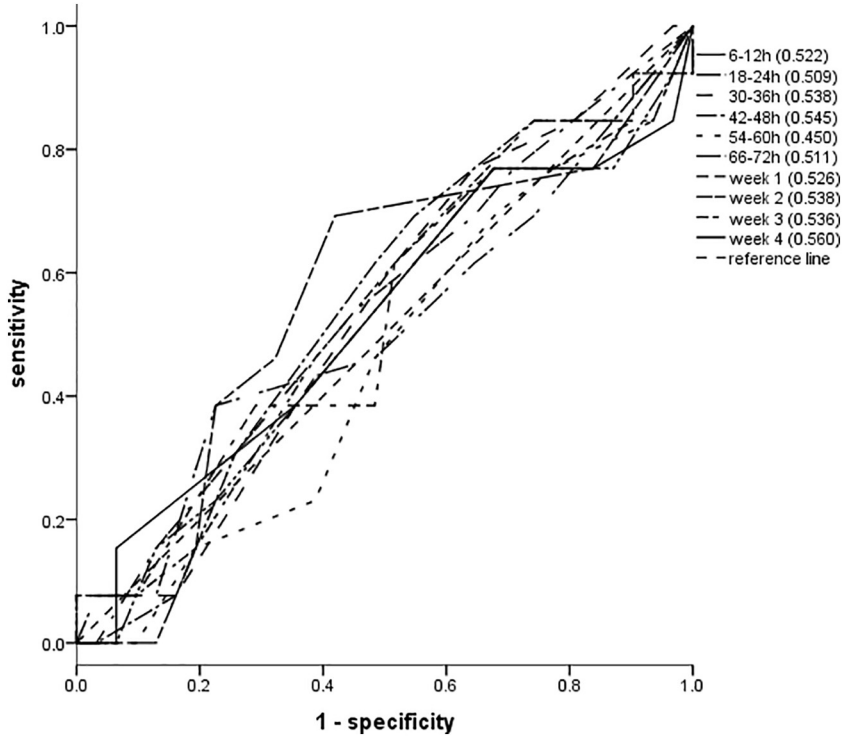

Fig. 2. Receiver operating characteristic curves calculated for all time periods for overall neurodevelopmental outcome. The area under the curve is in brackets.

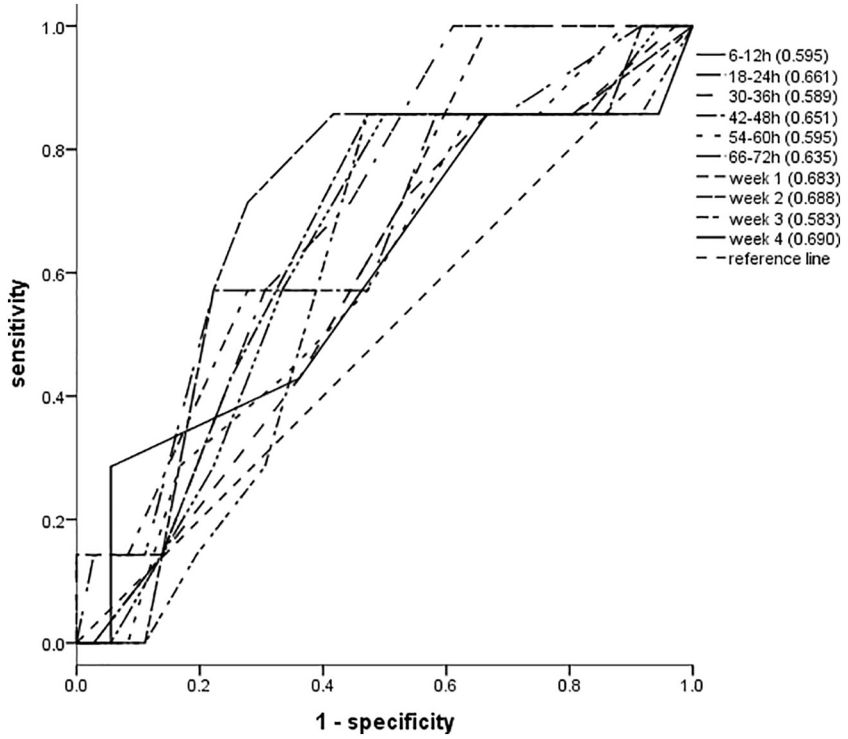

Fig. 3. Receiver operating characteristic curves calculated by psychomotor developmental index (PDI) for all time periods. The area under the curve is in brackets.

comparing infants with normal and delayed outcome in the first 72 h and the first 4 weeks of life. For cognitive outcome a significant difference between the groups was found only at day two of life. Klebermass et al. reported that one recording from the first week of life was not as good as a recording from the second week of life and speculated, that this might have reflected the potential influence of haemodynamic changes and of sedative/analgesic medication or methylxanthines on aEEG parameters during the first days of life, which might have lead to false positive rates of aEEG assessments early after birth [6,27]. A correlation of aEEG data at term equivalent age in preterm infants with a delayed development at 2 to 3 years has also been shown previously [6,9].

Despite the observed differences in aEEG signals in our study, the predictive value of the Burdjalov score regarding neurodevelopmental

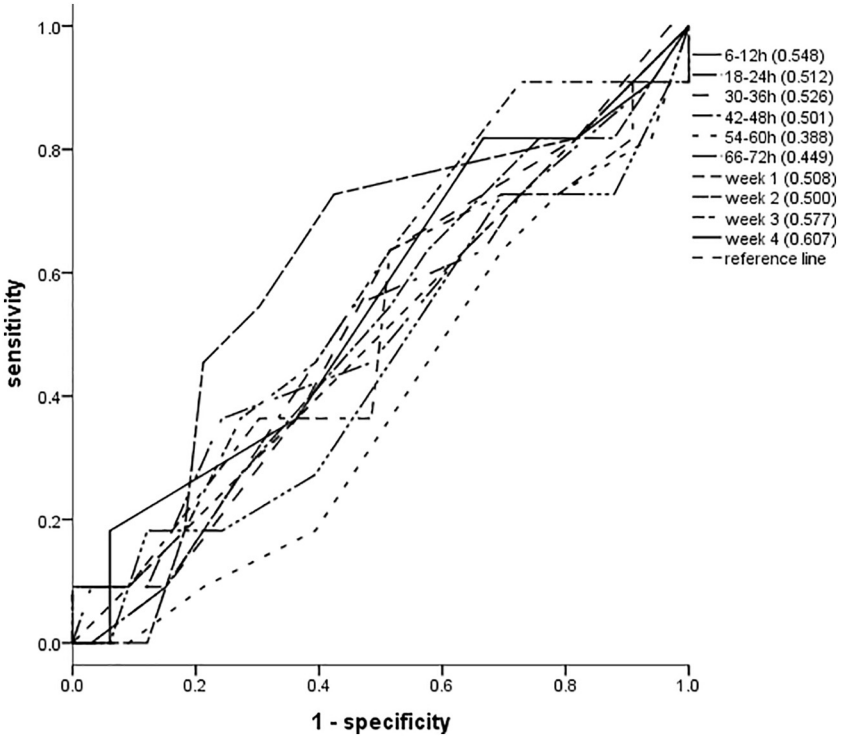

Fig. 4. Receiver operating characteristic curves calculated by mental developmental index (MDI) for all time periods. The area under the curve is in brackets.

outcome at the age of two in preterm infants was quite low. Our results suggest that neurodevelopment is complex and that outcome prediction should be performed more differentiated. This speculation is corroborated by Middel et al., showing coherences between aEEG and cognitive outcome, but not for psychomotor outcome at school age [5]. In a recent meta-analysis Fogtmann et al. concluded that aEEG might be useful to predict neurodevelopmental outcome in preterm infants, however, due to high risk of bias, further studies are needed [10]. However, in the studies revised by Fogtmann, aEEGs were performed only after parental consent as a scientific tool. Even though we could not find a high predictive value of aEEG in the preterm infant regarding neurodevelopmental outcome at the age of 2 years, this study adds valuable information, because at our department aEEG recording is part of the neonatal routine in preterm infants, which therefore offers a representative cohort. Our study population is highly representative, as there is no other hospital offering a neonatal intensive care unit in the geographical region.

Strengths of our study are the large study cohort, the prospective study design and the assessment of neurodevelopmental outcome by independent observers unaware of aEEG findings. Furthermore, aEEG recordings were conducted right after postnatal stabilisation, providing an early surveillance of electrocortical brain function. Regarding the fact that serial aEEG monitoring is a powerful method to assess brain development and health, the used approach to perform aEEG at numerous points during postnatal life is a strength of this study. Due to the mixture of infants scored by Bayley II and Bayley III, a composite score for infants scored by Bayley III was calculated as described previously [19]. A limitation of our study is that a separate analysis of the language score was not possible, but regarding our previous work about the prognostic value of the aEEG for literacy precursor skills this might be of interest for future studies [28]. We could not compare our current findings with our previous analysis at the corrected age of 1 year [11]. The reason was that we selected different survey periods, beginning with the time of routine aEEG evaluation at our department in the present study, in order to avoid any selection bias.

5. Conclusion

With this study, we found differences in aEEG parameters, using the Burdjalov score regarding neurodevelopmental outcome at the age of 2 years, exceptionally for psychomotor development. We cannot rule out that aEEG might be useful in preterm infants, but at present, it should not be suggested as routine method used to predict neurodevelopmental outcome.

Funding statement

This study did not receive any specific funding.

Author contributions

All authors have made substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work. All authors drafted the work or revised it critically for important intellectual content. All authors approved the final version of the manuscript.

Declaration of competing interest

There is no conflict of interest. All authors approved the final version of this manuscript before publication. The authors have no conflicts of interest to declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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