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REGULAR ARTICLE

Amplitude-integrated electroencephalography shows alterations in children born preterm displaying poor literacy precursor skills

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ABSTRACT

Aim: To assess whether amplitude-integrated electroencephalography (aEEG) alterations in the newborn period are associated with poor precursor skills of literacy at five years of age in children born preterm.

Methods: Between October 2007 and September 2011 248 preterm infants were eligible for the study at Innsbruck Medical University Hospital. aEEG was analysed for dominating background activity, calculation of the percentage of continuous activity, the Burdjalov scoring system, the minimum, mean and maximum amplitude. At the age of five years, we evaluated preterm born children by the Bielefelder screening (BISC) to assess for early diagnosis of reading problems and weak spelling and classified them as normal performers (n = 64) or poor performers (n = 20). Completion of testing was not possible for one infant.

Results: The minimum amplitude was significantly lower in the poor BISC performance group as compared to the normal BISC performance group at postnatal week two. The percentage of continuous background activity was significantly higher in infants with normal BISC performance than in infants with poor BISC performance at postnatal week three.

Conclusion: Children with poor developed precursor skills of literacy showed alterations in aEEG signals. The aEEG could be useful in further diagnosing preterm infants at risk for developmental complications.

INTRODUCTION

In preterm infants, the risk for short-term and long-term morbidity is still substantial and adverse neurological outcome is a frequent complication (1). Studies showed that language development is often impaired or delayed in children born preterm (2,3). In order to prepare plans for a timed management of infants with language and literacy difficulties at a preschool age, it would be desirable to single out children at risk for literacy deficits as early as the neonatal period (4).

Mehta et al. found that abnormalities in electroencephalography recordings are more frequent in infants with speech and language impairment (5). Event-related potentials are small parts of continuous electroencephalography recordings, which are evoked in response to stimuli and have been shown to be valuable in studying language processing or development and to predict literacy precursor skills. Paquette et al. reported that electrophysiological indicators, such as auditory event-related potentials and mismatch negativity, could be used in the neonatal period to predict atypical language processing later in life (3). So far, few studies investigated whether event-related potentials could be used to detect or predict cognitive impairments in preterm born infants and at present this method has not been applied in clinical practice in the neonatal period (6). Amplitude-integrated electroencephalography (aEEG) is a method of simplified electroencephalography monitoring and has become an important part of the neonatal routine in the last years (7,8). Studies indicated that the aEEG can be successfully exploited in preterm

Abbreviations
aEEG, Amplitude-integrated electroencephalography; BISC, Bielefelder screening; IQ, Intelligence quotient.

Key notes

- This study evaluated amplitude-integrated electroencephalography signals in children born preterm between 2007 and 2011 with poor developed precursor skills of literacy at the age of five years.
- We found that children with poor developed precursor skills of literacy showed alterations in amplitude-integrated electroencephalography signals in the first weeks of life.
- This study added information that amplitude-integrated electroencephalography might be regarded helpful to diagnose infants at risk for developmental complications.

infants and showed that continuous monitoring of brain activity via aEEG could provide prognostic information for impaired neurodevelopmental outcome (9–12). Reports showed that the aEEG could be used as a diagnostic measure of brain compromise, which causes changes of the amplitude and disturbances of the background pattern (7). As postulated by Wikström et al., neural dysfunction, reflected by alterations in electrocortical activity, could be a sign of developing brain damage (9). At early school age, Middle et al. evaluated the predictive value of aEEG in preterm infants and found some associations between aEEG amplitude centiles and cognitive outcomes (13). So far one published study has shown that the presence of seizure activity in the aEEG was related to lower language scores in preterm infants (14). Working from the hypothesis that differences in electrocortical activity were associated with risk for literacy deficits, this study was designed to evaluate whether alterations in aEEG signals in the newborn period were associated with impairment in precursor skills of literacy in children born preterm at the age of five years.

MATERIALS AND METHODS

Study design and participants

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, the only neonatal intensive care unit in the geographical region, were enrolled. The study was performed as retrospective analysis of prospectively collected data. The survey period was October 2007 to September 2011; 248 live births. The current study population formed 85 infants, who underwent cognitive and literacy precursor skill assessment (Fig. 1). Maternal and neonatal data were collected during hospital stay as described in our previous paper (15,16). Detailed information is given in Appendix S1.

aEEG recording and assessment

Two-channel aEEG was recorded with the BrainZ instruments BRM2 and BRM3 monitors (Natus Medical Inc, San Carlos, CA, USA) using hydrogel electrodes, with standard electrode placements at the C3, P3, C4 and P4 regions according to the 10–20 International System of Electrode Placement. This tool uses the parietal (P3, P4) electrodes for cross-cerebral aEEG recordings. The reference electrode is placed on the patient's back. Recording quality is monitored by continuous measurement of electrode impedance. The EEG signal is amplified and filtered through an asymmetric band pass filter, which attenuates activity below 2 and above 15 hertz. Processing of the aEEG signal includes semilogarithmic amplitude compression, by which the signal is displayed linearly from zero to 10 microvolts (mcV) and logarithmically from 10 to 100 mcV. The signal is then rectified, smoothed, time-compressed and displayed on the monitor on a semilogarithmic scale at a speed of 6 cm per hour.

The aEEG was assessed for dominating background activity, calculation of the percentage of continuous activity for each period and infant, qualitative visual assessment according to Burdjalov et al. and the minimum, mean and maximum amplitude values as described in our previous paper (15,17). Detailed information is given in Appendix S2.

Follow-up and assessment of literacy precursor skills

At our department, all infants born with a gestational age of <32 weeks at birth are regularly invited for follow-up visits until they enter school. The follow-up visit at five years of age includes an interview with the child's mother or other primary caregiver, a physical and neurological examination, and assessment of cognitive development using the German version of the Wechsler Preschool and Primary Scales of Intelligence, third edition as described in our previous paper (18). Additionally, children are evaluated with the Bielefelder screening (BISC) to assess for early diagnosis of reading problems and weak spelling, which is a standardised test for preschool children administered verbally (19). All cognitive tests were performed by one of three experienced psychologists (KK). This study was performed retrospectively, therefore in Austria no participant consent needed to be obtained. All examinations performed were part of the follow-up routine at our Department. The study was approved by the Ethics Committee of the Medical University of Innsbruck (Study No. AN2013-0086 333/4.2).

Statistical methods

Statistical analyses were performed using SPSS software version 24.0 for Windows (SPSS Inc., Chicago, IL, USA). For group comparisons of normally distributed continuous data, Student's *t*-tests were performed; for data not adhering to a particular distribution, Mann–Whitney *U* tests were applied. Categorical data were compared using the chi-square test. Data are presented as numbers with percentages, medians with interquartile range or means with standard deviation or 95% confidence intervals and their associated effect sizes. A logistic regression analysis was used to assess differences between preterm infants with normal and poor BISC outcome and potential confounders. Correlations were analysed using Kendal's Tau correlation coefficient. Results were regarded as statistically significant when two-sided $p < 0.05$.

RESULTS

Full-scale intelligence quotient (IQ) tests were performed at the age of five years. A normal (85 to 115 points) or high IQ (>115 points) scored 80 infants (94.1%). In total, five infants (5.9%) were classified as having cognitive delay (70 to 85 points). Substantial cognitive delay (<70 points) showed no child. Evaluation of nonverbal IQ scores showed that 94.0% reached normal (n = 66) or high (n = 12) nonverbal IQ rates. Five infants (5.9%) showed delay and no child showed significant delay in nonverbal performance.

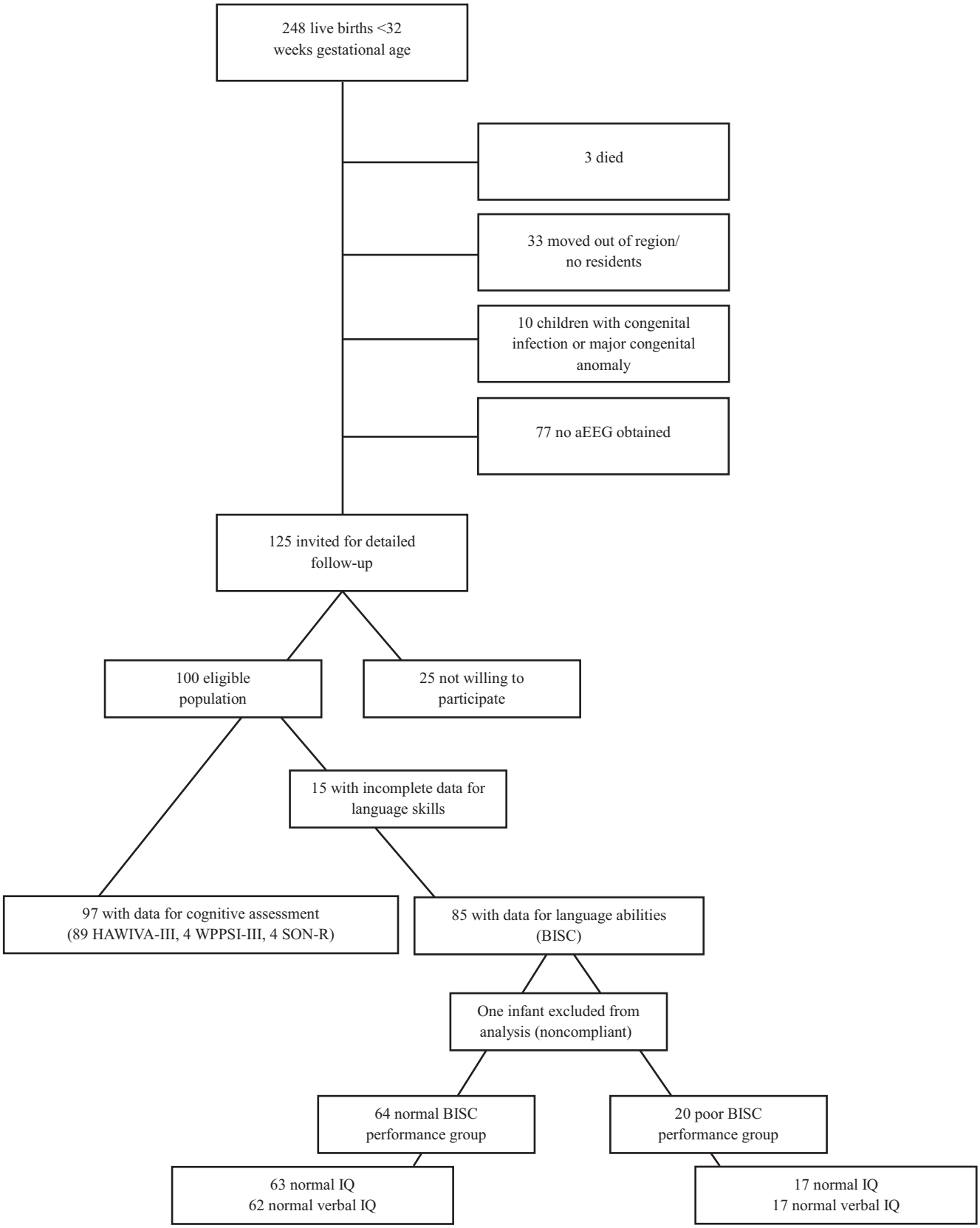

Figure 1 Flow chart: overview of children assessed for eligibility and enrolled in the study. SON-R = Snijders-Oomen nonverbal intelligence test, BISC = Bielefelder screening, IQ = intelligence quotient, WPPSI-III = Wechsler Preschool and Primary Scale of Intelligence, third edition.

Evaluation of verbal IQ scores revealed that 94.0% reached normal (n = 65) or high (n = 13) verbal IQ rates. Delay showed five infants (6.0%) and none of the 83 children showed significant delay in verbal performance.

A BISC test was performed in 85 (100%) children. Two infants were not able to finish BISC testing (noncompliant), of those one infant could not complete one subtest, but reached more than four risk points in the BISC assessment and was therefore classified as poor performer; the other infant was excluded from further analysis.

Normal performance showed 64 out of 84 infants (76.2%), nine infants borderline performance (10.7%) and 11 infants (13.1%) poor performance. In the normal performance group 63 infants scored a normal IQ (98.4%), one infant (1.6%) showed a mild delay; for verbal IQ 62 infants (96.9%) showed a normal verbal IQ, two infants (3.1%) a mild delay.

For infants showing borderline BISC performance, 100% scored a normal IQ and 88.9% a normal verbal IQ, one infant showed a mild delay (11.1%). In the poor BISC performance, group 17 out of 20 (85%) scored a normal IQ and 18 out of 20 (81.8%) a normal verbal IQ, two infants showed a mild delay (18.2%). For further analysis, infants were categorised as normal BISC performance (n = 84) and poor BISC performance (n = 20) (Fig. 1).

When correlating the results of the estimate full-scale IQ and the verbal IQ test with results from the BISC (BISC risk points), both coherences showed statistical significance (full-scale IQ r = −0.299 p = 0.001; verbal IQ r = −0.240, p = 0.009).

Table 1 summarises maternal, pre-, peri- and neonatal data in the normal (n = 64) and the poor (n = 20) BISC performance groups. Sociodemographic and neonatal characteristics were similar for both groups (Table 1).

Precursor skills of literacy and aEEG background activity

In both groups, the proportion of infants with continuous activity increased from 6–12 hours (7.4% versus 5.3%) to 66–72 hours of age (58.5% versus 66.7%) and further from week one (57.7% versus 66.7%) to week four (98.0% versus 87.5%). In infants with poor BISC performance, the percentage of continuous background activity was significantly lower at week three with a medium effect (U = 296, Z = −2.27, p = 0.023, r = −0.3) (Table 2). Logistic regression analysis showed consistent results after adjusting for antenatal steroids (ß coefficient −1.417, p = 0.063, OR 0.2 (0.05, 0.87).

Precursor skills of literacy and Burdjalov score

Figure 2 shows the total score (mean, 1 standard error of the mean) in both groups for all time points (Fig. 2). The total score tended to be lower in the poor BISC performance group, but did not reach statistical significance at any time point evaluated (6–12 hours p = 0.507, r = −0.1; 18–24 hours p = 0.200, r = −0.1; 30–36 hours p = 0.225, r = −0.1; 42–48 hours p = 0.715, r = −0.0; 54–60 hours p = 0.662, r = 0.0; 66–72 hours p = 0.796, r = 0.0; week one p = 0.521, r = 0.1; week two p = 0.617, r = 0.1; week three p = 0.299, r = 0.1; week four p = 0.143, r = 0.2). The separate scores are listed in Table 3. Infants with normal BISC performance showed significantly higher single scores

Table 1 Sociodemographic and neonatal characteristics in former preterm infants with normal and poor BISC performance

Variable	Normal BISC performance n = 64	Poor BISC performance n = 20	p value	Effect size
Gestational age (weeks) (mean)	29.79 ± 1.66	28.91 ± 2.28	0.125‡	0.028
Gestational age <28 weeks (n)	10 (15.6)	7 (35.0)	0.107†	0.205 (2.908;0.930–9.092)
Birthweight (g) (mean)	1256.75 ± 334.71	1138.25 ± 380.51	0.185*	0.484
Male (n)	24 (37.5)	11 (55.0)	0.166†	0.151 (0.491; 0.178–1.356)
Maternal age <23 years (n)	5 (7.8)	1 (5.0)	0.670†	0.047 (1.610; 0.177–14.654)
Maternal education <9 years (n)	3 (5.0)	2 (10.5)	0.389†	0.097 (2.235; 0.345–14.494)
Maternal education 9–12 years (n)	47 (78.3)	15 (78.9)	0.955†	0.006 (1.037; 0.294–3.666)
Maternal education ≥12 years (n)	10 (16.7)	2 (10.5)	0.516†	0.073 (0.588; 0.117–2.957)
Smoking in pregnancy (n)	13 (20.6)	4 (20.0)	0.951†	0.007 (0.962; 0.274–3.370)
1–10 cigarettes per day (n)	11 (100)	3 (75.0)	0.086†	0.443 (4.667; 1.712–12.724)
11–20 cigarettes per day (n)	0 (0.0)	1 (25.0)	0.086†	0.443 (0.214; 0.079–0.584)
Antenatal steroids (n)	49 (86.0)	19 (100)	0.084†	0.198 (1.388; 1.197–1.609)
Small for gestational age (n)	12 (18.8)	5 (25.0)	0.544†	0.066 (1.444; 0.439–4.753)
Surfactant treatment (n)	38 (60.3)	13 (68.4)	0.523†	0.071 (1.425; 0.479–4.244)
Intracerebral haemorrhage (n)	9 (14.1)	1 (5.0)	0.275†	0.119 (0.322; 0.038–2.709)
Intracerebral haemorrhage III–IV (n)	0 (0.0)	0 (0.0)		
Necrotizing enterocolitis (n)	3 (4.7)	3 (15.0)	0.118†	0.171 (3.588; 0.663–19.411)
Retinopathy of prematurity grade 3–4 (n)	1 (1.6)	2 (10.0)	0.076†	0.194 (7.000; 0.600–81.684)
Early-onset sepsis (n)	0 (0.0)	1 (5.0)	0.072†	0.196 (0.229; 0.154–0.340)
Late-onset sepsis (n)	5 (7.8)	3 (15.0)	0.339†	0.104 (2.082; 0.451–9.613)

Study group by outcome with n (%), mean (standard deviation), median (25th and 75th percentile). p values are from the chi-square test (†), Mann–Whitney *U* test (‡) or Student's t-test (*), as appropriate and effect sizes (eta square for Mann–Whitney *U* test; Cramers V with odds ratio and 95% CI for chi-square test; Cohen's D for Student's *t*-test). Information on maternal education could not be obtained in 5 (6%) subjects, information about administration of antenatal steroids was missing in eight (9.5%) subjects. In all other variables, the proportion of missing data was <5%.

Table 2 Proportion of infants with continuous background activity

	Normal BISC performance continuous activity (%), median (IQR)		Poor BISC performance continuous activity (%), median (IQR)		p value	r score
6–12 hours	7.4	0 (0;0)	5.3	0 (0;0)	0.752‡	−0.0
18–24 hours	28.3	0 (0;0)	16.7	0 (0;0)	0.330‡	−0.1
30–36 hours	34.0	0 (0;1)	22.2	0 (0;0.25)	0.357‡	−0.1
42–48 hours	42.9	0 (0;1)	38.9	0 (0;1)	0.772‡	−0.0
54–60 hours	50.0	0 (0;1)	64.3	1 (0;1)	0.350‡	−0.1
66–72 hours	58.5	1 (0;1)	66.7	1 (0;1)	0.585‡	−0.1
week 1	57.7	1 (0;1)	66.7	1 (0;1)	0.536‡	−0.1
week 2	75.0	1 (0.25;1)	62.5	1 (0;1)	0.328‡	−0.1
week 3	91.7	1 (1,1)	68.8	1 (0;1)	**0.023**‡	−0.3
week 4	98.0	1 (1,1)	87.5	1 (1;1)	0.086‡	−0.2

Percentage of continuous background activity, median (IQR) at each time point by group.
‡Mann–Whitney *U* test. Significance is provided correctly p = 0.023; bold values show significance levels (p < 0.05).

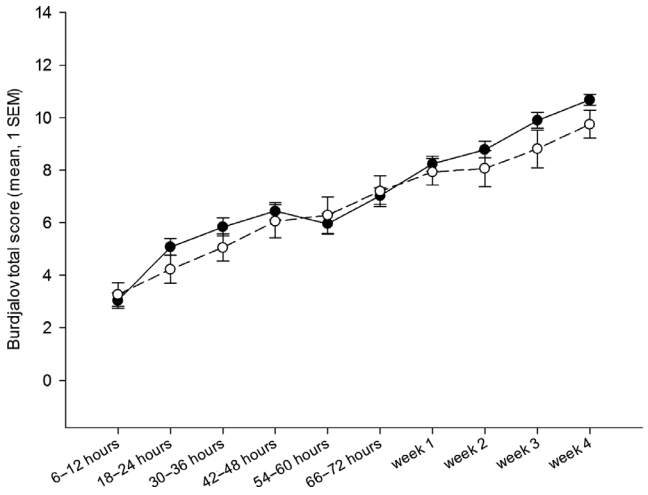

Figure 2 Burdjalov total score. Total score presented as mean ± 1 standard error of the mean, at each time point by group. Solid line: normal Bielefelder screening (BISC) performance group, dotted line: poor BISC performance group.

for the continuity parameter at postnatal week three with a small effect (U = 288, Z = −2.01, p = 0.044, r = −0.2) and at postnatal week four with a medium effect (U = 310, Z = −2.49, p = 0.033, r = −0.3) as compared to infants with poor BISC performance. Logistic regression analysis showed consistent results after adjusting for antenatal steroids at week three (ß coefficient −1.324, p = 0.041, OR 0.3 (0.1, 0.9) and at week four (ß coefficient −1.906, p = 0.041, OR 0.1 (0.02, 0.9).

Precursor skills of literacy and aEEG amplitudes

Mean and maximum amplitudes did not significantly differ between the two groups. The minimum amplitude tended to be lower in infants with poor BISC performance during the first 60 hours and from week two to week three. This difference showed significance only at week two with a small effect (U = 275, Z = −2.12, p = 0.034, r = −0.2) (Fig. 3A–C). Logistic regression analysis showed consistent results after adjusting for antenatal steroids (ß coefficient −0.745, p = 0.027, OR 0.5 (0.2, 0.9).

DISCUSSION

Amongst all aspects of poor outcome in preterm infants, language development is commonly impaired (2). Previous studies indicated that infants with poor language performance at school age show abnormalities in electrocortical signals already in the neonatal period (3,6). Mehta et al. showed that abnormalities in conventional EEG are present in 64.5% of infants with speech and language impairment (5). Wikström et al. showed that an abnormal background pattern in the aEEG predicted poor neurological outcome at the age of two in children born preterm (9). The present study investigated differences in aEEG signals in the first four weeks after birth in preterm infants with normal and with poor performance in the BISC test battery for precursor skills of literacy at a preschool age. For this purpose, the visual background activity, the Burdjalov score and minimum, mean and maximum amplitude parameters were compared between children born preterm with normal and those with poor BISC performance at the age of five years. With regard to precursor skills of literacy, we were the first to show that percentage of continuous background activity was significantly lower at week three in infants with poor BISC performance. Wikström et al. suggested that during the first 72 hours of life aEEG amplitudes are decreased in infants with neonatal brain injury and that lower amplitudes were associated with a disturbed neurodevelopmental function at age two (20). In accordance with Wikström et al., we observed that in the poor performance group, the minimum amplitude was significantly lower than in the normal performance group at postnatal week two. As published in one of our studies, a predictive value of the Burdjalov Score for neurodevelopmental outcome assessed by the Bayley Scales of Infant Development in preterm infants was confirmed (21). Concordant with those findings, we found that infants with poor BISC performance had a significantly lower single score for continuity than did infants with normal BISC performance. Furthermore, we observed that infants with poor BISC performance had a lower Burdjalov total score as compared to infants with normal BISC performance and that the poor performance group reached the level of the normal performance group only at three evaluation points and scored higher at no time. This observation did not reach statistical significance and needs to be confirmed in larger studies.

So far, there has been only one study published focusing on aEEG and language development. Vesoulis et al. showed that the presence of seizures during the first 72 hours in preterm infants was associated with lower language scores at the age of two (14). Due to the fact that

Table 3 Burdjalov single parameters

	Normal BISC performance median (IQR)	Poor BISC performance median (IQR)	p value	r score
Continuity				
6–12 hours	0.00 (0.00;1.00)	0.00 (0.00;1.00)	0.873‡	−0.0
18–24 hours	1.00 (0.00;1.00)	1.00 (0.00;1.00)	0.478‡	−0.1
30–36 hours	1.00 (0.00;2.00)	1.00 (0.00;1.00)	0.223‡	−0.1
42–48 hours	1.00 (1.00;2.00)	1.00 (0.00;2.00)	0.325‡	−0.1
54–60 hours	2.00 (1.00;2.00)	2.00 (0.75;2.00)	0.674‡	−0.0
66–72 hours	2.00 (1.00;2.00)	2.00 (1.00;2.00)	0.867‡	−0.0
Week 1	2.00 (1.00;2.00)	2.00 (1.00;2.00)	0.565‡	−0.1
Week 2	2.00 (1.00;2.00)	2.00 (1.00;2.00)	0.763‡	−0.1
Week 3	2.00 (2.00;2.00)	2.00 (1.00;2.00)	**0.044**‡	−0.2
Week 4	2.00 (2.00;2.00)	2.00 (1.25;2.00)	**0.013**‡	−0.3
Cycling				
6–12 hours	1.00 (0.00;1.00)	1.00 (0.00;1.00)	0.983‡	−0.0
18–24 hours	1.00 (1.00;2.00)	1.00 (0.00;2.00)	0.242‡	−0.1
30–36 hours	2.00 (1.00;2.00)	1.00 (1.00;2.00)	0.113‡	−0.2
42–48 hours	2.00 (1.00;2.00)	2.00 (1.00;2.25)	0.669‡	−0.0
54–60 hours	2.00 (1.00;2.00)	2.00 (1.00;2.00)	0.526‡	−0.1
66–72 hours	2.00 (1.00;2.00)	2.00 (1.00;3.00)	0.728‡	−0.0
Week 1	3.00 (2.00;3.00)	2.00 (2.00;3.00)	0.259‡	−0.1
Week 2	3.00 (2.00;3.00)	2.50 (2.00;3.75)	0.536‡	−0.1
Week 3	3.00 (3.00;4.00)	3.00 (2.00;4.00)	0.661‡	−0.0
Week 4	4.00 (3.00;4.00)	3.00 (2.25;4.00)	0.147‡	−0.2
Amplitude of lower border				
6–12 hours	1.00 (0.00;1.00)	1.00 (0.00;1.00)	0.701‡	−0.0
18–24 hours	1.00 (1.00;2.00)	1.00 (1.00;2.00)	0.163‡	−0.2
30–36 hours	2.00 (1.00;2.00)	2.00 (1.00;2.00)	0.577‡	−0.1
42–48 hours	2.00 (1.50;2.00)	2.00 (1.00;2.00)	0.441‡	−0.1
54–60 hours	2.00 (2.00;2.00)	2.00 (1.00;2.00)	0.172‡	−0.2
66–72 hours	2.00 (2.00;2.00)	2.00 (2.00;2.00)	0.596‡	−0.1
Week 1	2.00 (2.00;2.00)	2.00 (2.00;2.00)	0.717‡	−0.0
Week 2	2.00 (2.00;2.00)	2.00 (1.00;2.00)	0.084‡	−0.2
Week 3	2.00 (2.00;2.00)	2.00 (2.00;2.00)	0.970‡	−0.0
Week 4	2.00 (2.00;2.00)	2.00 (2.00;2.00)	0.080‡	−0.2
Amplitude of lower border and bandwidth span				
6–12 hours	1.00 (0.00;1.00)	1.00 (0.00;1.00)	0.529‡	−0.1
18–24 hours	1.00 (1.00;2.00)	1.00 (1.00;1.25)	0.101‡	−0.2
30–36 hours	2.00 (1.00;2.00)	2.00 (1.00;2.00)	0.585‡	−0.1
42–48 hours	2.00 (1.50;2.00)	2.00 (1.00;2.00)	0.290‡	−0.1
54–60 hours	2.00 (2.00;2.00)	2.00 (1.00;2.00)	0.236‡	−0.1
66–72 hours	2.00 (2.00;2.00)	2.00 (2.00;2.00)	0.718‡	−0.0
Week 1	2.00 (2.00;3.00)	2.00 (2.00;3.00)	0.416‡	−0.1
Week 2	2.00 (2.00;3.00)	2.00 (1.00;3.00)	0.337‡	−0.1
Week 3	3.00 (2.00;3.00)	3.00 (2.00;3.00)	0.180‡	−0.2
Week 4	3.00 (3.00;4.00)	3.00 (2.00;4.00)	0.372‡	−0.1

Score (median, IQR: interquartile range) at each time point by group.
‡Mann–Whitney *U* test.

not all of our monitors were equipped with the automatic seizure detection algorithm and that in our cohort no clinical seizures or sudden changes in the upper or lower margin of the aEEG were detected, we could not compare their findings to our cohort. Of importance Vesoulis et al. assessed early language scores at the age of two, but using the Bayley Scales of Infant Development III, a score that combines the assessment of mental, motor and behavioural development at a rather early stage of development (22).

Our study has some limitations. We did not assess professional, but only school education of the mother, which is part of our standardised follow-up evaluation. Furthermore, maternal substance abuse could not be further assessed in detail, based on the fact that only self-reported data (written down in the so-called mother–child booklet, the official Austrian pregnancy and early childhood medical record book in Austria) could be evaluated. Another limitation is that this study was not designed as

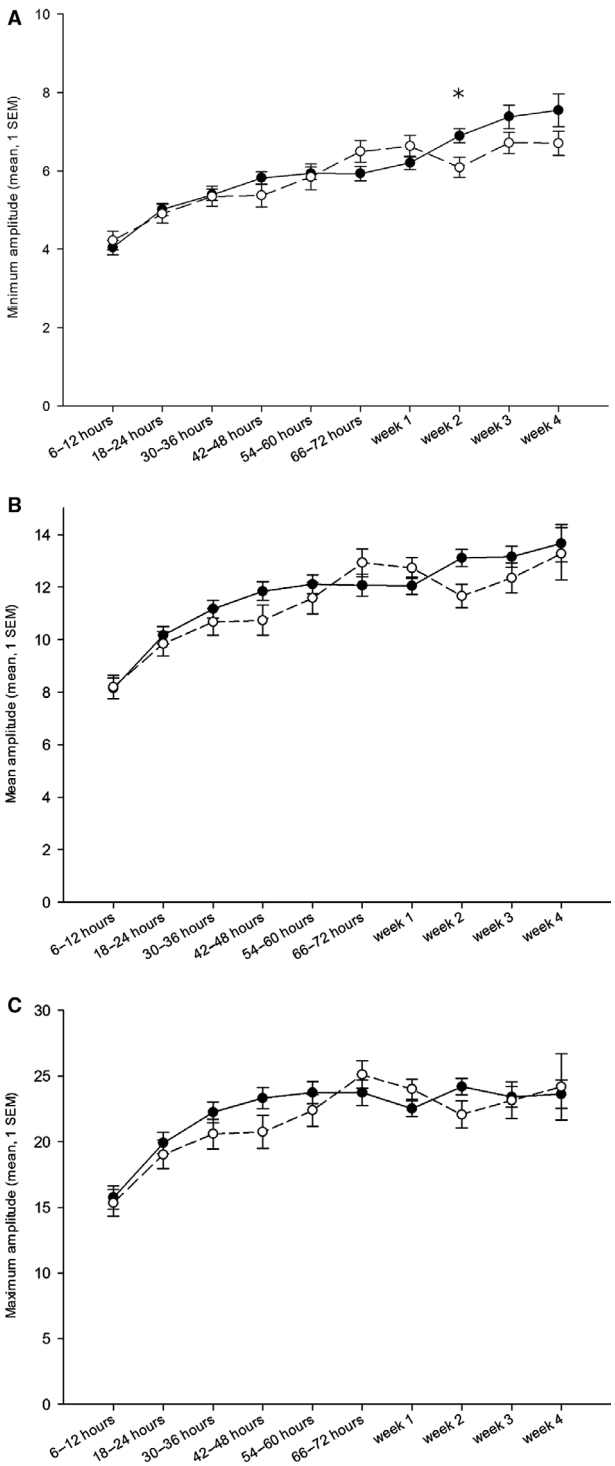

Figure 3 (A–C) Amplitude parameters: Minimum, mean and maximum amplitude presented as mean ± 1 standard error of the mean, at each time point by group. Solid line: normal Bielefelder screening (BISC) performance group, dotted line: poor BISC performance group. *$p < 0.05$.

such and therefore not sufficiently powered to incorporate gestational age as clinical variable associated with poor outcome. However, the two groups of infants did not differ significantly in the gestational age or the number of infants per group with a gestational age below 28 weeks. This study was performed as a retrospective analysis of retrospectively collected data. We invited all eligible infants for a detailed follow-up visit, which is optional and included 85 infants with data for language abilities. We chose the study period a priori, to avoid potential confounding factors that could develop based on changes in neonatal care (such as introduction of the less invasive surfactant administration technique). Based on the fact, that statistical power was not estimated a priori, we report effect sizes for all tests that were carried out, in order to allow the reader to estimate the replicability of our findings.

The early postnatal conduction of aEEG recordings right after initial stabilisation of the infants is strength of this study. Another strength of our study is that we chose to investigate children born preterm at the age of five years by using the BISC, which is a well-established test battery to particularly assess precursor skills of literacy (19,23).

CONCLUSION

There is considerable evidence that children at risk for literacy deficits at a preschool age showed differences in aEEG parameters already in the neonatal period. In line with our previous study, which demonstrated that aEEG in preterm infants was able to predict neurodevelopmental outcome at one year of age, the current study showed that alterations in aEEG signals were related to poor developed precursor skills of literacy at the age of five years. Further studies are needed focusing on a detailed evaluation about the predictive value of these findings, taking into account potential confounders and on the optimal time at which to perform aEEG in preterm infants in order to predict infants with literacy deficits. Further evaluations of aEEG signals might provide more insight into the prediction of complications in this area and could help tailor developing early support strategies for children with literacy deficits.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1 Maternal and neonatal data.
Appendix S2 aEEG recording and assessment.

