Journal of Integrative Neuroscience

*J. Integr. Neurosci.* **2024**; 23(8): 150
https://doi.org/10.31083/j.jin2308150

*Original Research*

# Diagnostic Accuracy of the Persyst Automated Seizure Detector in the Neonatal Population

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Academic Editor: Imran Khan Niazi
Submitted: 30 March 2024 Revised: 7 June 2024 Accepted: 13 June 2024 Published: 19 August 2024

**Abstract**

**Background**: Neonatal seizures are diagnostically challenging and predominantly electrographic-only. Multichannel video continuous electroencephalography (cEEG) is the gold standard investigation, however, out-of-hours access to neurophysiology support can be limited. Automated seizure detection algorithms (SDAs) are designed to detect changes in EEG data, translated into user-friendly seizure probability trends. The aim of this study was to evaluate the diagnostic accuracy of the Persyst neonatal SDA in an intensive care setting. **Methods**: Single-centre retrospective service evaluation study in neonates undergoing cEEG during intensive care admission to Great Ormond Street Hospital (GOSH) between May 2019 and December 2022. Neonates with <44 weeks corrected gestational age, who had a cEEG recording duration >60 minutes, whilst inpatient in intensive care, were included in the study. One-hour cEEG clips were created for all cases (seizures detected) and controls (seizure-free) and analysed by the Persyst neonatal SDA. Expert neurophysiology reports of the cEEG recordings were used as the gold standard for diagnostic comparison. A receiver operating characteristic (ROC) curve was created using the highest seizure probability in each recording. Optimal seizure probability thresholds for sensitivity and specificity were identified. **Results**: Eligibility screening produced 49 cases, and 49 seizure-free controls. Seizure prevalence within those patients eligible for the study, was approximately 19% with 35% mortality. The most common case seizure aetiology was hypoxic ischaemic injury (35%) followed by inborn errors of metabolism (18%). The ROC area under the curve was 0.94 with optimal probability thresholds 0.4 and 0.6. Applying a threshold of 0.6, produced 80% sensitivity and 98% specificity. **Conclusions**: The Persyst neonatal SDA demonstrates high diagnostic accuracy in identifying neonatal seizures; comparable to the accuracy of the standard Persyst SDA in adult populations, other neonatal SDAs, and amplitude integrated EEG (aEEG). Overdiagnosis of seizures is a risk, particularly from cEEG recording artefact. To fully examine its clinical utility, further investigation of the Persyst neonatal SDA's accuracy is required, as well as confirming the optimal seizure probability thresholds in a larger patient cohort.

**Keywords:** electroencephalogram; EEG; seizure; automated detection; neonate; intensive care; status epilepticus

## 1. Introduction

Seizures present more often during the neonatal period than any other time of life, with an incidence of 1–5 per 1000 live births and are therefore associated with increased morbidity or mortality [1,2]. Increased excitability in the immature, developing brain leads to an increased susceptibility to seizures, but the developing brain may also be more susceptible to injury from the seizures themselves [3,4]. In neonates with hypoxic-ischaemic encephalopathy (HIE), a higher seizure burden has been associated with increased severity of brain injury on magnetic resonance imaging (MRI), and poor neurodevelopmental outcome independently of other factors [5,6]. The effect of seizure burden on outcome in other seizure aetiologies is less clear. However, a similar association with poorer outcomes has been reported in older children with status epilepticus [7,8]. Effective and timely treatment with anti-seizure medications may reduce the extent of brain injury and improve neurodevelopmental outcomes [9,10]. However, the effect of treatment on long-term outcomes has varied between studies and is still debated [11]. Most crucially, early treatment with anti-seizure medications is associated with a better response rate and reduced seizure burden [9,12,13].

Timely treatment requires accurate and prompt identification of seizures, which can prove challenging in the neonatal population. Up to 50–80% of neonatal seizures are electrographic-only, detectable only on electroencephalogram (EEG) with no clinical manifestation [14,15]. Seizures with EEG and clinical correlation may become uncoupled after anti-seizure treatment leading to ongoing electrical seizure activity with no corresponding clinical signs [16,17]. Conversely, overtreatment may occur in the absence of EEG monitoring when other neonatal movements can be misdiagnosed as seizures. Treatment with anti-seizure medications comes with its own risks of side effects such as respiratory depression and hypotension,

and some have also been associated with adverse neurodevelopmental outcomes [14,18]. Multichannel, video continuous electroencephalography (cEEG) is the gold standard investigation for neonatal seizure detection, consisting of a minimum of 24 hours of monitoring for neonates at-risk of seizures or with a clinical suspicion [15,19]. However, most hospitals have limited access to cEEG, or out-of-hours clinical neurophysiology support, thus restricting the possibility for timely identification of seizures and treatment [20,21]. Amplitude-integrated EEG (aEEG) is widely used in neonatal units as an alternative or adjunct to cEEG which can be more easily interpreted by trained nurses and intensivists [22]. A systematic review showed aEEG has a 76% sensitivity for identifying neonatal seizures, however, it may still not detect seizures of short duration or focal seizures originating outside the parietal/central aEEG channel regions [23,24].

Automated seizure detector algorithms (SDAs) have been designed as an adjunct tool to aid real-time cEEG review at the bedside and provide prompt seizure recognition. The algorithm analyses multiple different inputs from cEEG recordings and determines the probability that a section of cEEG represents an electrographic seizure. This probability is then displayed in a simple graphical format and may include an audible alarm to alert clinicians [25,26]. Given the simple alert system, theoretically this could be used by clinicians with no EEG training to interpret the result and use this to direct further cEEG review and clinical management [27,28]. This may be particularly useful for centres without limited or no out-of-hours access to clinical neurophysiology expertise. It can also be used by neurophysiologists as an adjunct to other trends to speed up cEEG review [29,30].

Seizure detector algorithms have undergone rapid development over the last few decades, most recently with the incorporation of deep learning technologies training the algorithms on large EEG datasets. Most algorithms utilise a full cEEG montage although some are designed for use with simplified aEEG channels [25,28,31]. A number of SDAs have been designed for and tested in neonatal populations, including Algorithm for Neonatal Seizure Recognition (ANSeR), Stellate EEG system and Brainz 'Recognize' algorithms. These have demonstrated sensitivity in seizure detection which is comparable to aEEG and would require less training to use [32]. The Persyst 14 (P14) SDA for use in adult patients has been available since 2020 but was not optimised for use in the neonatal population [26,33]. More recently, the research version of P14 made a neonatal-specific SDA available which has been trained on neonatal cEEG recordings. This neonatal SDA is now available as a standard tool in Persyst 15 (P15) [26]. The aim of this study was to evaluate the accuracy of the Persyst neonatal SDA to identify electrographic seizures in neonatal patients in an intensive care setting.

## 2. Materials and Methods

### *2.1 Study Design and Participants*

This was a single-centre retrospective service evaluation study using cEEG recordings from neonatal patients admitted to three intensive care units (neonatal-NICU, paediatric-PICU, or cardiac-CICU) at Great Ormond Street Hospital (GOSH) from 1st May 2019 to 31st December 2022. Neonates undergoing neurophysiology review during their admission were identified from the electronic patient record database (Epic) and then screened for inclusion criteria. Patients were eligible for inclusion if they fulfilled the following criteria: (1) <44 weeks corrected gestational age at the time of the cEEG recording; (2) Inpatient in any of the three GOSH intensive care units at the time of the cEEG recording; (3) cEEG recording duration >60 minutes. The neurophysiology reports were then reviewed to select those with seizures detected during this recording (cases) and those that were seizure-free (controls). Once categorized, a random number generator was used to select controls from this list to equal the total number of cases identified. Demographic data and clinical details of the patients were also collected from the electronic patient records.

### *2.2 Creation of cEEG Clips*

All cEEG recordings were previously collected using Natus NeuroWorks EEG Software (versions 7.0–9.0, Natus, Middleton, WI, USA) during routine clinical care and stored on archive hard drives in the neurophysiology department. If a patient had multiple cEEGs, only the first cEEG that met the above inclusion criteria was used for the study.

An expert Clinical Neurophysiologist review of the recordings was used as the gold standard for diagnosis of seizures. This was obtained retrospectively using the neurophysiology report from electronic patient records and annotations on the cEEG recording, which were used to identify the start time of the first seizure. The full cEEG recording, video data and clinical presentation were available to the clinical neurophysiologist for this review, as is standard in routine clinical care. The cEEG clips of the cases were independently reviewed by author MC who had access to the cEEG data but was blinded to video recordings and clinical context.

A 60-minute clip of each cEEG recording was created using the pruning feature on Natus [34], starting as close to the start of the original recording as possible (controls) or within 1–10 minutes of the first seizure (cases).

### *2.3 Persyst Seizure Detector Settings and Output*

The Persyst neonatal SDA (available in the research version of P14, Persyst, Solana Beach, CA, USA) was used for this study. This SDA uses advanced neural network technology and has been trained on prolonged scalp EEG recordings from approximately 150 seizure seizure-affected neonates, collected from six institutions and marked by

multiple readers. In addition, approximately 50 other neonatal records without seizures were used for training, including training of a patting artifact detection algorithm. At the time of writing, the Persyst neonatal SDA (available only in the research version of P14) had not yet received regulatory approval as a medical device. However, it is anticipated that the version to be released for clinical use (as part of Persyst 15, USA) will have US FDA approval and conformite europeenne (CE) marking (EU MDR 2017/745). It is also important to note that none of the test data evaluated in this study were used during training of the neonatal SDA.

The detector uses data from 10–20 system EEG recording electrodes, modified for neonates, in a 13-channel double distance anterior-posterior bipolar montage plus channels C3-Cz and C4-Cz. Various software sensors and concepts are processed using advanced neural network technologies. Examples include assessments of power, frequency, bandwidth, and asymmetry by channel; segmentation and evolution of rhythmic activity in four frequency bands (0.66–2.66, 2.66–5.33, 5.33–8.0, 8.0–21.3 Hz); signal change points via use of empirical null statistics; patting artifact detection via neural network; and various seizure-related concepts including seizure, seizure onset, post-ictal changes, and identification of seizure candidates including seizure onset and cessation points. Thus, many features and concepts are evaluated for each channel. For example, the convolutional seizure neural network for channel C3-O1 has approximately 100 inputs. A nested hierarchy of feed forward neural networks ultimately outputs seizure detections, each described by its onset, offset, and probability. The algorithm's analyses proceed in one-second increments, using information before the current one-second epoch to estimate the probability of seizure activity; seizure probability outputs can be updated for several minutes beyond a particular segment as more EEG data become available.

As an alternative to the standard reduced neonatal electrode recording montage, a smaller electrode subset including sites Fp1/2 (or alternate F1/2), C3/4, and O1/2 in a bipolar montage (utilizing: Fp1-O1, Fp2-O2, C3-C4) can be utilized for seizure detection, or an even smaller two-channel montage of C3-Cz and C4-Cz. However, some loss of sensitivity and increase in false positive rate can usually be expected when using these further reduced montages, especially the two-channel variant. The Persyst neonatal SDA settings can be adapted for each centre, with adjustments according to the standard montages in use. Four different settings were used in this study to adapt the SDA for use on the retrospective clinical recordings at GOSH (see **Supplementary Material**). The 'SeizureProbability (Neonatal)' calculation engine was added and the 'SeizureProbabilityP14' and 'SeizureEventsP14' trends were selected and displayed in the Persyst trends panel. The neonatal SDA was initially run on five randomly selected case and control cEEG recordings to test the settings, before each case and control cEEG clip was then processed.

Each cEEG clip was analysed to determine the accuracy of Persyst to identify the presence or absence of seizures in the 60-minute recording. The highest seizure probability value for each cEEG clip was then used to calculate the sensitivity and specificity of the seizure detector at different probability cut-offs and produce a Receiver Operating Characteristic (ROC) curve.

### *2.4 Statistical Analysis*

IBM SPSS Statistics 27 (IBM, Armonk, NY, USA) was used for all statistical analysis during this study. Case and control groups were unpaired. Patient demographic numeric data were tested for normality of distribution using visual inspection of histograms and Q-Q plots, and the Kolmogorov-Smirnov and the Shapiro-Wilk tests for normality. Mean, standard deviation and a Two-sample *T*-test were used for normally distributed numeric data. Median, range and Mann-Whitney U tests were used for non-normally distributed numeric data. Categoric variables were described using percentages and compared using the Chi-square test. A threshold of statistical significance was set as a $p$ value of $<0.05$ for all tests. The ROC area under the curve (AUC) and 95% confidence intervals were reported. Youden's index was calculated to identify the optimal cut-off probability. A post-hoc analysis of Persyst setting usage was compared between the case and control groups.

## 3. Results

A search of the electronic patient record (Epic) produced a list of 580 individual EEG patients who were screened for eligibility. In total, 273 patients met inclusion criteria: 51 of these with seizures, 222 without seizures. The prevalence of seizures (within the population of patients eligible for the study) was approximately 19%. Subsequently, two neonates were excluded from the cases group due to lack of clear consensus on the diagnosis in the neurophysiology report. This provided 49 cases for the study and a random number generator was used to select 49 controls (see Fig. 1).

Demographics and clinical characteristics of the case and control groups are shown in Table 1. Statistically significant differences were noticed for gestational age at birth and corrected gestational age at time of presentation. There was no statistically significant difference noticed between the two groups for any of the other clinical variables. This included no statistically significant difference in the use of different Persyst montages and channel mapping settings between the two groups in a post-hoc analysis

The commonest seizure aetiology for case patients was hypoxic ischaemic injury (17 patients—35%). This group could be further subdivided into two major causes: hypoxic ischaemic injury secondary to severe congeni-

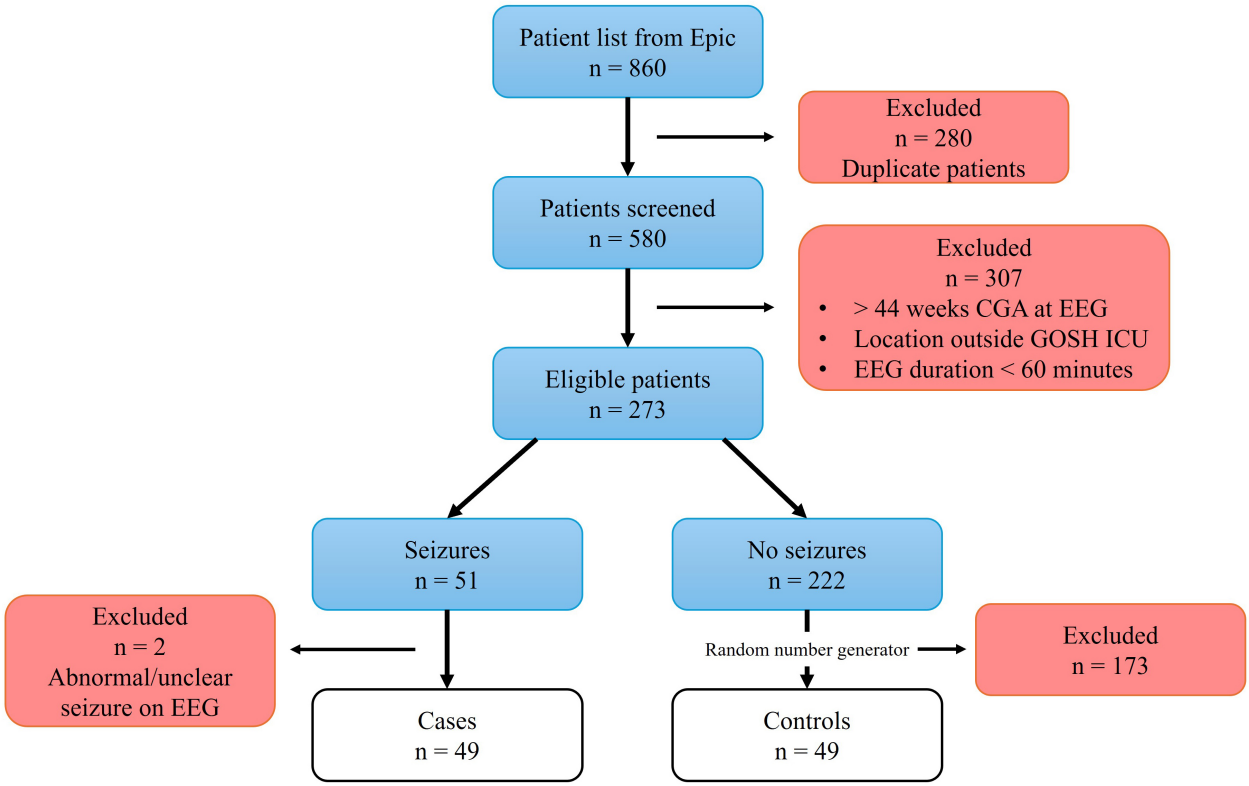


**Fig. 1. Flow diagram of study eligibility screening.** CGA, Corrected Gestational Age; EEG, Electroencephalography; GOSH, Great Ormond Street Hospital; ICU, Intensive Care Unit; n, number.

tal heart disease or cardiac arrest (11 patients—22% of all seizure cases), and hypoxic ischaemic encephalopathy following an event in the immediate perinatal period (6 patients—12% of all seizure cases). Metabolic (including inborn errors of metabolism) was the second commonest cause (9 patients—18%), followed by vascular (8 patients—17%), structural/cerebral malformations (7 patients—14%), central nervous system (CNS) infection (4 patients—8%), genetic/epileptic encephalopathies (3 patients—6%) and unknown (1 patient—2%).

The maximum seizure probability produced by Persyst for each case and control is shown in Fig. 2. Most cases showed a spike of high seizure probability and most controls showed only low probabilities. Outliers were identified in both groups (see Fig. 2).

The ROC curve in Fig. 3 demonstrates the diagnostic accuracy of the Persyst seizure probability output at different thresholds. The AUC was 0.94 (95% confidence interval (CI), 0.889 to 0.988). Calculation of Youden's index identified the optimal probability thresholds for diagnostic accuracy as 0.4 (sensitivity 84%, specificity 94%, Youden's index 0.78) and 0.6 (Sensitivity 80%, Specificity 98%, Youden's index 0.78).

The ROC curve analysis subdivided by different Persyst settings is shown in Fig. 4. The Persyst setting details are described in further detail in the **Supplementary Material**.

## 4. Discussion

The results of this study showed good diagnostic accuracy of the Persyst neonatal SDA in identifying seizures in this neonatal population. Based on a seizure probability threshold of 0.6, the algorithm produced a sensitivity of 80% and specificity of 98%. This demonstrated similar accuracy to a previous study of the standard P14 SDA in adult patients (sensitivity 78%), other neonatal seizure detectors (sensitivities ranging from 66–93% and specificities 78–88%), as well as alternatives such as aEEG (sensitivity 76%) [24,32,33,35]. The Persyst neonatal SDA has been trained on and uses a 10-channel double-distance montage to analyse seizure probabilities. As a result, it avoids the limitations of the simplified aEEG montages, which can miss some focal or shorter duration seizures, while still being user-friendly to non-expert reviewers [23–25]. This therefore presents an excellent tool in neonatal units with limited out-of-hours access to neurophysiology support, to alert clinicians to possible seizures requiring further neurophysiology review.

### *4.1 Selection of Probability Thresholds*

The probability thresholds of 0.4 and 0.6 were identified as the optimal probability cut-offs to balance sensitivity with specificity. The selection of cut-offs may depend on the planned utilisation of the SDA. If the seizure de-

**Table 1. Demographics and Clinical Characteristics of the study patients.**

| | | Cases | Controls | *p*-value |
|---|---|---|---|---|
| Demographics | | | | |
| Birth weight (grams), *Mean (SD)* | | 3060.5 (792.2) | 2790.0 (845.1) | 0.105 |
| Birth GA (weeks), *Median (Range)* | | 38.3 (25.3–42.1) | 37.6 (23.9–42.3) | 0.047* |
| CGA at EEG (weeks), *Mean (SD)* | | 40.2 (2.4) | 39.0 (2.8) | 0.028* |
| Age at EEG (days), *Median (Range)* | | 11.0 (0–82) | 8.0 (0–72) | 0.799 |
| Male sex, *n (%)* | | 27.0 (55.1) | 28.0 (57.1) | 0.839 |
| Clinical Characteristics | | | | |
| Ventilated, *n (%)* | | 42.0 (85.7) | 41.0 (83.7) | 0.779 |
| Cardiovascular support, *n (%)* | None, *n (%)* | 22.0 (44.9) | 24.0 (49.0) | 0.913 |
| | Inotropes, *n (%)* | 22.0 (44.9) | 20.0 (40.8) | |
| | ECMO, *n (%)* | 5.0 (10.2) | 5.0 (10.2) | |
| Mortality in ITU, *n (%)* | | 18.0 (36.7) | 17.0 (34.7) | 0.833 |

SD, Standard Deviation; GA, Gestational Age; CGA, Corrected Gestational Age; EEG, Electroencephalography; ECMO, Extracorporeal Membrane Oxygenation; ITU, Intensive Care Unit; n, number; *$p$ value $< 0.05$.

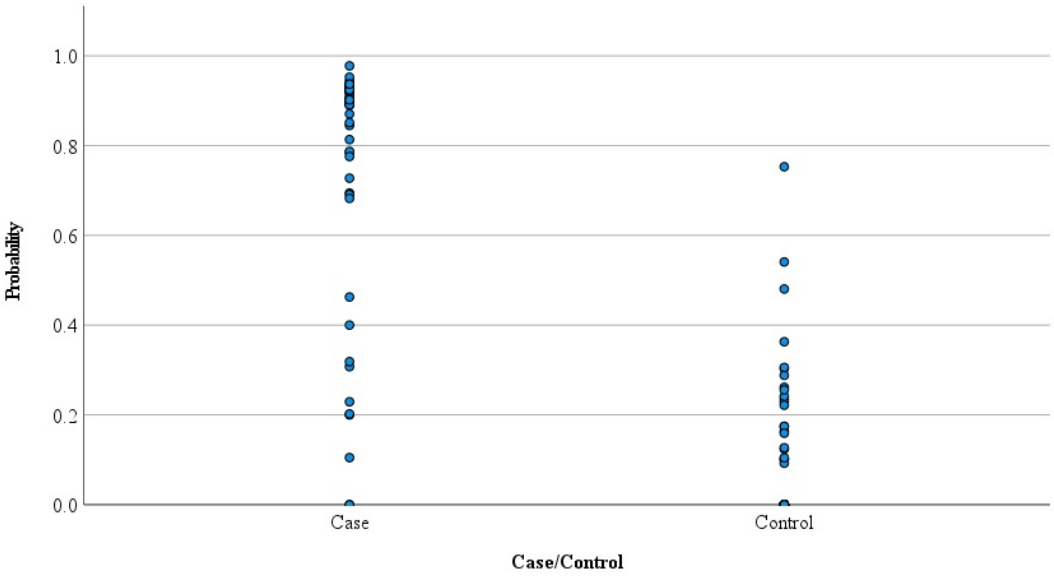


**Fig. 2. Dot plot of highest seizure probability for each case and control.**

tector were to be used as a decision support tool to guide clinicians to start anti-seizure medications, then a probability cut-off with a higher specificity is required to prevent overtreatment of false positive results. A probability threshold of 0.6 (sensitivity 80%, specificity 98%) or higher would therefore be optimal. For a threshold above 0.8, the sensitivity was significantly reduced to 65% but specificity was 100%, highly suggesting that anti-seizure medications should be started when the seizure probability is above this threshold. Conversely, if the detector were to be used as a screening tool to alert clinicians, who will first review the raw cEEG data or request neurophysiology review, then a lower probability threshold of 0.4, producing a higher sensitivity of 84%, would be important to avoid non-detection of seizures. This would accept a slightly lower specificity but would expect any false positives to be screened out by expert review. A lower probability threshold, with even higher sensitivity but lower specificity, would not be advised as too many alerts from false positives could lead to alarm fatigue and a reduced response [36].

### *4.2 Comparison with Previous Studies*

A study of the standard P14 SDA in adult patients by Scheuer *et al*. [33] showed an average sensitivity of 78% (Standard deviation, SD 33.9) with 0.97 false positives per day (SD 1.81), a sensitivity which is comparable to our results using the neonatal SDA at a probability threshold of 0.6. However, Scheuer *et al*. [33] used a fixed probability threshold of 0.8, which produced a much lower sensitivity (but 100% specificity) in the study's population. This dis-

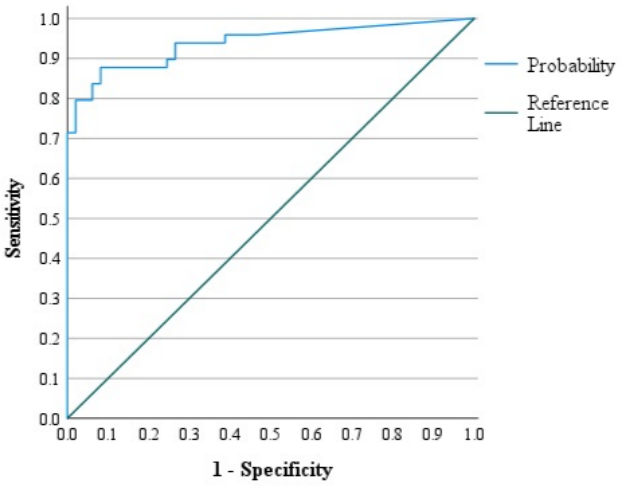


**Fig. 3. ROC curve of seizure probability for all study recordings.** ROC, receiver operating characteristic.

parity could be due to differences in the study population, or the montages and settings used, but it demonstrated the benefit of adjusting the seizure probability to customise detection for a specific population or patient. It also indicated that testing and adapting the Persyst neonatal SDA to each population would be essential prior to use, rather than using standard settings.

Previous versions of the Persyst seizure detector have also been tested in adult and paediatric populations. The Persyst 13 (P13) algorithm showed a high sensitivity (74–83% in different studies) but much higher false positive rate (11.3–15.5 false positives per day) [33,36]. A comparison of the Persyst 11 (P11) and two other algorithms, ICTA-S and NB (Stellate Harmonie Version 7), in paediatric intensive care patients, identified P11 as the most accurate with a sensitivity of 76% and false positive rate of 5.1 per day. All other detectors showed either unacceptably low sensitivity or high false positive rates [36]. The Persyst 12 (P12) algorithm has been tested in a mixed adult and paediatric population and demonstrated a similar sensitivity to its P11 counterpart, but also noted the effects of seizure pattern and morphology on its accuracy. The P12 was most sensitive for generalised onset seizures and less able to identify focal, low frequency, low amplitude seizures. Therefore, it was suggested that after identifying the seizure pattern and morphology on first seizure for an individual patient, further review of the EEG could be customised using the addition of other quantitative EEG trends to optimise seizure detection [31]. This would be more relevant to adaptation of the Persyst algorithm for neurophysiology review, rather than as a screening tool for clinician seizure detection at the bedside. Adaptations of the P14 SDA in comparison to earlier models are reported to include improved accuracy, a shorter latency to allow faster detection of seizures, a visual graph of seizure probability trend displayed against time, and more adjustable settings including the selection of the seizure probability threshold for an alert [26,33]. The Persyst EEG Software company have recently released a new software version, P15, which incorporates the neonatal seizure detector as a standard tool [26]. The P15 neonatal SDA is largely like the P14 neonatal counterpart (available only in the research version) that was evaluated in this study and further use in varied neonatal populations will build on the current understanding of its accuracy.

Other SDAs have been more extensively tested in neonatal populations including the ANSeR, Stellate EEG system and Brainz 'Recognize' algorithms. The ANSeR algorithm, developed by the Irish Centre for Fetal and Neonatal Translational Research (INFANT) Research Centre in Cork has been designed specifically for neonatal seizures and has similarly adjustable probability settings. Initial tests of the detector using probability thresholds of 0.5 and 0.3, demonstrated a sensitivity of 53–75% and false detection rates of 0.04–0.36 per hour, in a study of 35 cases and 35 controls [32]. Subsequently, a multicentre randomised controlled trial (RCT) in neonatal patients compared an 'algorithm group' which used both cEEG and ANSeR for review, to a 'non-algorithm group' where the cEEG alone was analysed. There was no statistically significant difference between the two groups—sensitivity was 81% in the algorithm group compared to 90% in non-algorithm, specificity 84% and 89%, false detection rate 37% and 23%, respectively. However, this demonstrates the high accuracy of the ANSeR algorithm in neonatal seizure detection which may be even more beneficial in neonatal units with limited clinical neurophysiology cover or experience in cEEG interpretation [37].

Overall, the present study showed comparable, if not more accurate, results to other SDAs. However, differences in study design, including different patient populations and the analysis of detection of individual seizures, may make direct comparison to this study's data more challenging. The ANSeR RCT demonstrated the real-world utility of a similar SDA to the Persyst neonatal SDA and suggested the potential next step in determining its benefits in clinical practice.

### *4.3 Limitations*

This is a retrospective single-centre study with a relatively small number of cases and controls. However, larger case numbers are difficult to achieve given the incidence of neonatal seizures.

At the time of the study being conducted, the Persyst neonatal SDA was not yet in clinical use in our centre. This necessitated retrospective channel mapping to adapt cEEG recordings to be recognised by Persyst. This may have limited accuracy, particularly in the recordings that could only use the limited 2-channel montage in Persyst, but post-hoc analysis comparing these settings did not demonstrate a statistically significant difference. The decision to analyse the detection of the presence or absence of seizures in a 60-

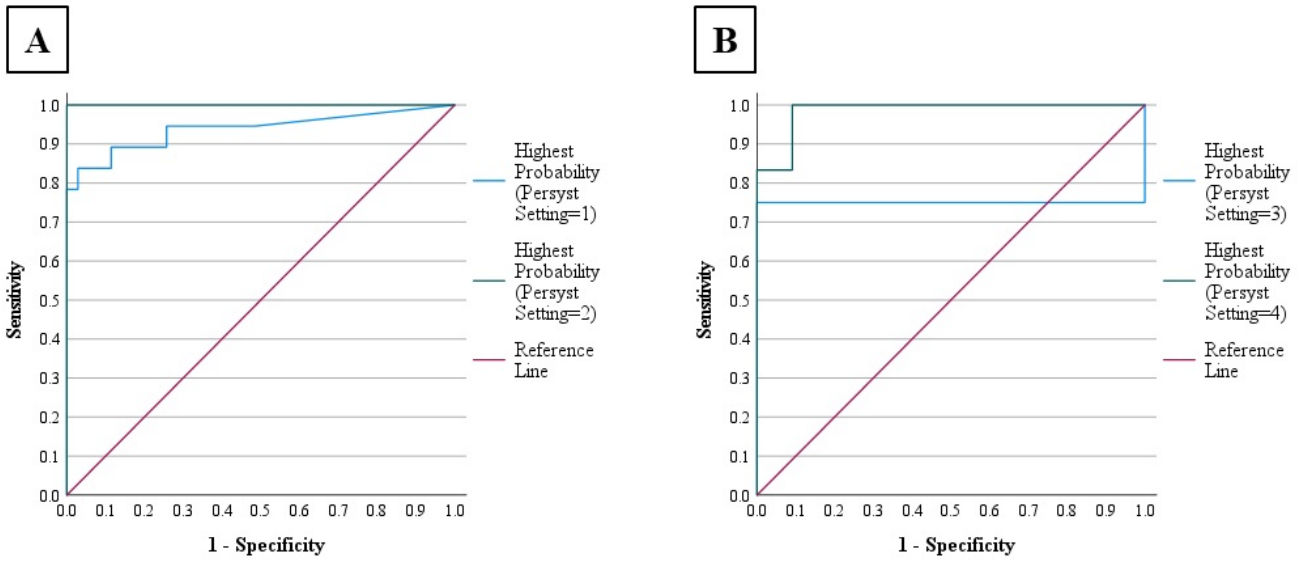


**Fig. 4. ROC curve of seizure probability subdivided by Persyst settings.** (A) Study recordings using Persyst setting 1 (light blue) and setting 2 (dark blue line). (B) Study recordings using Persyst setting 3 (light blue) and setting 4 (dark blue line).

minute recording, rather than the detection of each individual seizure, may have also affected the accuracy of the analysis, as did limiting the volume of cEEG data tested by the algorithm to 60 minutes per patient. However, this analysis still provides clinically useful information about early detection of seizures within 60 minutes, a short enough time limit to start appropriate anti-seizure treatment. The algorithm always starts an assessment of the EEG recording in the first few minutes to establish its baseline and its accuracy then strengthens as it continues to run. Therefore, seizures occurring in the first few minutes of the recording may be missed by the algorithm, potentially producing bias in the data. Running the study on longer recordings, as well as analysing accuracy for each individual seizure, would be beneficial for further validation of the algorithm's accuracy.

The study was conducted at GOSH, a quaternary centre with a somewhat different neonatal population compared to maternity neonatal services, as also demonstrated by the case seizure aetiology. There was a comparatively low percentage of patients with HIE, which usually accounts for up to 65% of seizure aetiology versus 35% of the cases here. Of this 35%, only approximately one-third is due to acute perinatal events, whereas this is the predominant cause of hypoxic ischaemic injury in other centres [38]. Morphology and location of seizures can be influenced by the underlying seizure aetiology which could potentially affect the accuracy of the Persyst neonatal SDA if applied to a different population [15,23]. Similarly, prematurity and immature brain development affects the EEG background and seizure characteristics [23,39]. Most of the cases and controls were term corrected gestational age at the time of the EEG, and of the small number still preterm, all were >30 weeks at the time of the EEG. This study therefore does not test the SDA's accuracy for seizure detection in extremely or very preterm neonates. Further studies of the Persyst neonatal SDA in different populations are needed, particularly in maternity neonatal services with a higher number of preterm and HIE patients compared to our centre.

The cEEG recordings in this study were obtained during admission to intensive care, thus increasing the risk of artefact interference from devices and other monitors, and hence over-interpretation of seizures by the algorithm. Further interrogation of the cEEG recordings showed poor signal quality or artefacts in cases and controls which were identified as outliers (see Fig. 2). The Persyst neonatal SDA's accuracy regardless of this risk of artefacts, demonstrates its utility in neonatal populations where most patients at risk of seizures will be admitted to an intensive care unit for monitoring.

## 5. Conclusions

This study demonstrated the high diagnostic accuracy of the Persyst neonatal seizure detector to identify neonatal seizures in an intensive care setting and supported further investigation of this software as a useful clinical diagnostic tool in the neonatal population. Accuracy may be affected by artefact leading to a possible risk of over-diagnosis of seizures. To prevent over-treatment with anti-seizure medications, its most appropriate clinical use currently would be as a screening tool to prompt further neurophysiology review. To fully determine its clinical utility, further investigation is required focusing on the Persyst neonatal SDA's accuracy for individual seizure detection, as well as confirming the optimal seizure probability thresholds in a larger cohort of patients.

## Abbreviations

ANSeR, Algorithm for Neonatal Seizure Recognition; aEEG, amplitude-integrated electroencephalography; AUC, area under the curve; cEEG, continuous electroencdephalography; CGA, corrected gestational age; EEG, electroencephalography; ECMO, extracorporeal membrane oxygenation; GA, gestational age; GOSH, Great Ormond Street Hospital; HIE, hypoxic ischaemic encephalopathy; ITU, intensive care unit; MRI, magnetic resonance imaging; RCT, randomised controlled trial; ROC curve, receiver operating characteristic curve; SDA, seizure detection algorithm; SD, Standard Deviation.

## Availability of Data and Materials

All data points generated or analysed during this study are included in this article and there is no further underlying data necessary to reproduce the results.

## Author Contributions

ED, RP and MC designed the research study. ED performed the research, analysed the data and wrote the manuscript under the guidance of MC. DM, KH and SB provided neurophysiology technical support and advice. MC independently reviewed the cEEG recordings of the cases. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

This study was registered as a Service Evaluation Project with the Clinical Audit Department at Great Ormond Street Hospital (GOSH) who reviewed the project and assigned it as exempt from requiring full ethics approval. Consent forms were therefore not required. A unique registration number 3379 was assigned to the study with the original title: Evaluation of automated seizure detection algorithm in critically ill neonates. The study was conducted in accordance with the institutional ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975.

## Acknowledgment

The authors would like to acknowledge a number of people who helped and supported this project: Duncan Shepherd and the Epic data team for providing the initial list of EEG patients; Michael Guess at Persyst for providing technical support for the initial set-up of the Persyst P14 seizure detector software; the Persyst EEG Software company for providing the Persyst P14 Research program as a free trial for a limited period of time, enabling us to undertake this study; the wider GOSH multidisciplinary team who helped to care for the neonatal patients in this study, and in particular, a thank you to the Clinical Neurophysiology department for their help and support throughout this project.

## Funding

This research received no external funding.

## Conflict of Interest

The authors ED, DM, KH, SB, and MC declare no conflict of interest. RP is serving as co-chair of the ILAE Pediatrics Commission task force ‘Guideline on Neonatal Seizures’. RP reports personal fees and non-financial support from NATUS, personal fees from UCB, during the conduct of the study; personal fees from GW; from null, outside the submitted work.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.jin2308150.

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