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Electroencephalography during acute painful procedures in neonates: a scoping review

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Abstract

Although electroencephalography (EEG) is used to assess neonatal pain in research settings, EEG assessments have not been sufficiently characterized for use as end points to assess the efficacy of analgesics in regulatory-endorsed, industry-sponsored trials. We aimed to identify all studies conducted in neonates with EEG recordings during acute somatic nociceptive skin-breaking procedures, and to create a network of authors who will be invited to contribute their individual participant data (IPD) to an IPD meta-analysis to establish the validity, reliability, and clinical interpretability of an EEG-based neonatal pain measure. To identify literature, we searched MEDLINE, Embase, CINAHL, Web of Science, Scopus, Google Scholar, ClinicalTrials.gov, and the WHO ICTRP from database inception to July 2, 2025. Eligible studies were primary empirical studies that included neonates with EEG recordings during acute skin-breaking procedures. We identified 55 studies across 11 countries. Heel lance was the most common painful procedure; others included venipuncture, immunization, and lumbar puncture. The impact of 12 analgesic interventions has been studied to date, mostly nonpharmacological interventions. Individual-electrode EEG is more common than EEG caps. We noted relatively high data loss due to EEG data-quality concerns. A wide range of non-EEG pain-relevant measures have been recorded alongside EEG (eg, behavior, vital signs). Coauthorship network analysis highlighted that authors commonly work within discrete authorship hubs, with limited coauthorship across hubs. The predominance of studies was from European and American institutions, which limits generalizability. We conclude that sufficient data are available to undertake an IPD meta-analysis.

Keywords: Pain, EEG, Neonate, Evidence synthesis

1. Introduction

Neonatal pain assessment is extremely challenging. This is due to (1) the subjective nature of painful experiences, (2) the nonverbal nature of neonates, and (3) a lack of specificity of behavioral and physiological responses to painful and non-painful stimuli.[75] Development of clinical pain scales for neonates and infants has been ongoing since at least the late 1980s, with more than 40 different versions currently available to both the clinician and the researcher.[15,58] Many of these pain scales rely on more than one measurement "domain," such as a combination of measures from the behavioral (eg, facial expressions, limb movements), the cardiovascular (eg, heart rate, blood pressure), or the respiratory (eg, breathing pattern, oxygen requirement) domains. However, over the past decade, there has been increased interest among both researchers[11,86] and regulatory bodies[36,88] in the development of brain-based indicators of neonatal pain for use as a primary end point in clinical trials or as a component of a multidimensional neonatal pain scale.

Currently, brain-based indicators are not included in neonatal pain scales. This is likely due to both limited access to brain-based equipment for monitoring or evaluating pain responses and the lack of well-established validity, reliability, and clinical interpretability of these measures.[2,3] Owing to these concerns and the desire to advance clinical pain scale content validity,[26] we are undertaking an individual participant data (IPD) meta-analysis of an electroencephalography (EEG) metric.[9] The overarching goal is to facilitate the creation of an EEG-based acute pain pharmacodynamic biomarker for use in neonates.[9] We are specifically interested in acute somatic nociceptive pain, where pain is defined as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.[51] We operationalize acute pain as acute somatic skin-breaking procedures (eg, heel lance procedures), which is in line with acute pain models for clinical trials in the neonatal population recommended by the ACTTION (Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks) Pediatric Pain

Research Consortium.[106] Compared with standard summary data meta-analyses, an IPD meta-analysis enables the ability to perform more powerful and nuanced analysis of the source data, while facilitating the analysis of larger sample sizes than in individual studies.[78] Furthermore, this approach will enable the implementation of standardized analytic techniques to establish the measurement properties of an EEG-based acute pain biomarker.

As an initial step toward conducting the IPD meta-analysis, we scoped existing literature to identify researchers who have recorded EEG in neonates during acute skin-breaking procedures and who may have relevant individual neonatal EEG data that could contribute to the IPD meta-analysis. Our intention is to create a collaborative network of researchers sharing data to empower others to develop novel EEG-based methods and outcomes. In this current scoping review, we have (1) summarized the relevant literature, (2) invited investigators who conducted relevant studies to coauthor the review and provide expertise and insights on factors affecting data quality and study design, and (3) developed a standardized and objective approach to facilitate future collaborative efforts.

We identified the primary empirical research conducted on acute neonatal pain that featured EEG as a recording method. We report on where and when this research has been conducted and catalog researchers working in this field. We summarize the: (1) sample sizes of the studies that collected EEG data, (2) age and sex distributions of study participants, (3) nature of the collected EEG data, (4) painful procedures that were investigated, and (5) pain relief interventions that have been studied using EEG outcomes to date. To understand the heterogeneity in collected EEG data and the potential for implementing a standardized analytic approach as part of the IPD meta-analysis, we also document the electrode placement methods and positions. To address concerns about data quality when using neonatal EEG for pain research, we quantify the amount of data reportedly lost due to EEG data quality issues. Finally, we record non-EEG pain assessment measures that were collected alongside the EEG data, including clinical pain scales, vital signs measurements, and pain behavior videos.

2. Methods

2.1. Research question

We aimed to identify all published research on pain in neonates assessed using EEG and bring together this research community. This scoping review is the initial stage of an IPD meta-analysis designed to assess the reliability, validity, and clinical interpretability of a specific EEG outcome measure.[9] The associated IPD meta-analysis research question is "Is the specific EEG-recorded brain activity magnitude metric under investigation, that is evoked by acute somatic nociceptive skin-breaking procedures in neonates 34–44 weeks postmenstrual age (PMA), a reliable, valid, and interpretable pain-relevant indicator?" The eligibility criteria (see below) are the same in this scoping review as in the IPD meta-analysis, except we do not restrict the participants' age to 34 to 44 weeks PMA. Instead, the entire neonatal period is included in this scoping review. The neonatal period for term and post-term neonates is defined as the day of birth plus 27 days; the neonatal period for preterm neonates is defined as the day of birth through the expected date of delivery plus 27 days.[30,31] The search strategies (see below) are identical between the IPD meta-analysis and the scoping review.

Because this scoping review is the first stage of the IPD meta-analysis, the research question is similar to the IPD meta-analysis research question. The scoping review research question in PICO

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

A complete list of INC Pain Working Group members appears in the Acknowledgments.

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(Population, Intervention, Comparator, Outcome) format includes (1) human neonates as population, (2) acute somatic nociceptive skin-breaking procedure as "intervention" ie, painful procedure, (3) comparator is not applicable, and (4) EEG measures of procedure-evoked brain activity. The research question is "What research has been published examining acute somatic nociceptive skin-breaking procedures in human neonates, assessed using EEG?"

2.2. Protocol development

This scoping review is a subcomponent of the IPD meta-analysis protocol, which has been written according to PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Protocol extension) guidelines,[67] has been pre-registered on PROSPERO (International Prospective Register of Systematic Reviews) on July 14, 2023 (CRD42023444809), and has subsequently been published in a peer-reviewed journal.[9] No data extraction for this scoping review occurred before review registration on PROSPERO.

2.3. Eligibility criteria

We provide a full list of our eligibility criteria in the Supplementary Information (Supplementary Table 1, http://links.lww.com/PR9/A400). We included primary empirical research studies, including gray literature, with any study design and without any restriction related to publication date or language. We excluded secondary literature (eg, reviews, book chapters) and nonempirical publications (eg, commentaries, opinions, perspectives).

2.4. Literature searches

We searched 6 bibliographic databases: MEDLINE (Ovid), Embase (Ovid), CINAHL (EBSCO Industries), Web of Science Core Collection (Clarivate Analytics), Scopus (Elsevier), and Google Scholar (Publish or Perish). We searched the clinical trial registry ClinicalTrials.gov (https://clinicaltrials.gov) and the clinical trial registry platform WHO ICTRP (World Health Organization International Clinical Trials Registry Platform; https://trialsearch.who.int), which includes 18 registries. Finally, we included publications known to the authors. All databases and trial registry platforms were searched from inception to July 2, 2025.

For electronic searches, the search strategy was initially developed in MEDLINE, then translated for other databases and registries. The search focused on the combination of 3 core topics: "neonate," "pain," and "EEG." The search strategies were independently peer-reviewed using the PRESS Checklist by an Outreach Librarian at the Bodleian Health Care Libraries, University of Oxford.[63] All search strategies are presented in full in the Supplementary Information, http://links.lww.com/PR9/A400.

We used EPPI-Reviewer (Evidence for Policy and Practice Information and Co-ordinating Reviewer) for deduplication and screening.[97] Study selection was a 2-stage process: screening on title and abstract followed by screening on full text. Screening was performed in duplicate by 2 independent reviewers and disagreements settled by discussion between both reviewers.

2.5. Data extraction and variable explanation

Data extraction was performed by one author and then verified by a second author, with disagreements settled by discussion. The data extraction and synthesis were only performed on a single representative publication per research study. In instances where a study had multiple associated publications (eg, one clinical trial had a trial registration, a protocol paper, a statistical analysis plan paper, a main publication paper, and an additional trial report document), a single primary publication representative of the study was selected for data extraction and synthesis. We extracted data on publication year, country in which data were collected, authorship, sample size, average age of participants, sex ratio, skin-breaking procedures, pain-relief interventions, EEG electrode placements, EEG data quality issues, and non-EEG data. Explanations for each of these variables are provided in the Supplementary Information (Supplementary Table 2, http://links.lww.com/PR9/A400).

2.6. Data synthesis

We synthesized data descriptively; we did not perform inferential statistics or hypothesis testing. Results are presented primarily as figures. The researcher coauthorship network was produced using VOSviewer.[28]

3. Results

3.1. Study selection and study characteristics

Of the 2,355 records screened, we identified 76 relevant to this review (**Fig. 1**). Twenty-one of 76 (26.9%) were directly related to the same study with multiple publication types (eg, clinical trial registrations for completed trials and published articles). In all cases, there was a clear primary publication, with additional publications excluded from synthesis including trial registrations, theses, conference abstracts, preprints, protocols, and statistical analysis plans. A list of the 21 nonprimary publications excluded from synthesis is provided in the Supplementary Table 3, http://links.lww.com/PR9/A400.[5,8,10,13,16,19,22,27,38,39,56,64,65,68,76,81,87,89,90,96,101] A list of the 55 unique representative primary publications included in the synthesis is provided in the Supplementary Table 4, http://links.lww.com/PR9/A400.[1,4,6,12,14,17,18,20,21,23,24,32–35,37,40–47,50,53–55,57,60–62,69–74,77,79,80,84,85,91–93,95,99,100,103–105,107,109,110]

3.2. Results structure

Below, we first outline the geographical origin of the EEG data and the publication year of the relevant records for the 55 unique studies included in the synthesis. Second, we assess the coauthorship network of these studies, excluding the 7 trial registrations (as there is no authorship list for trial registrations), which resulted in a total of 48 studies for coauthorship network analysis. Third, we provide details on study populations of neonates, EEG sample sizes and acquisition details, painful procedures, analgesic interventions, and non-EEG outcomes, for all 44 studies containing analyzable EEG details. Eleven of 55 studies without analyzable EEG details included: (1) 7 trial registrations,[23,37,57,70,71,74,107] (2) 3 methods development articles with vaguely detailed exemplar EEG data,[35,109,110] and (3) one clinical trial protocol (Supplementary Table 4, http://links.lww.com/PR9/A400).[17]

3.3. Geographical and temporal distribution of research

Of the 55 unique studies, most data were collected in Europe, with the United Kingdom (UK) producing the highest number of

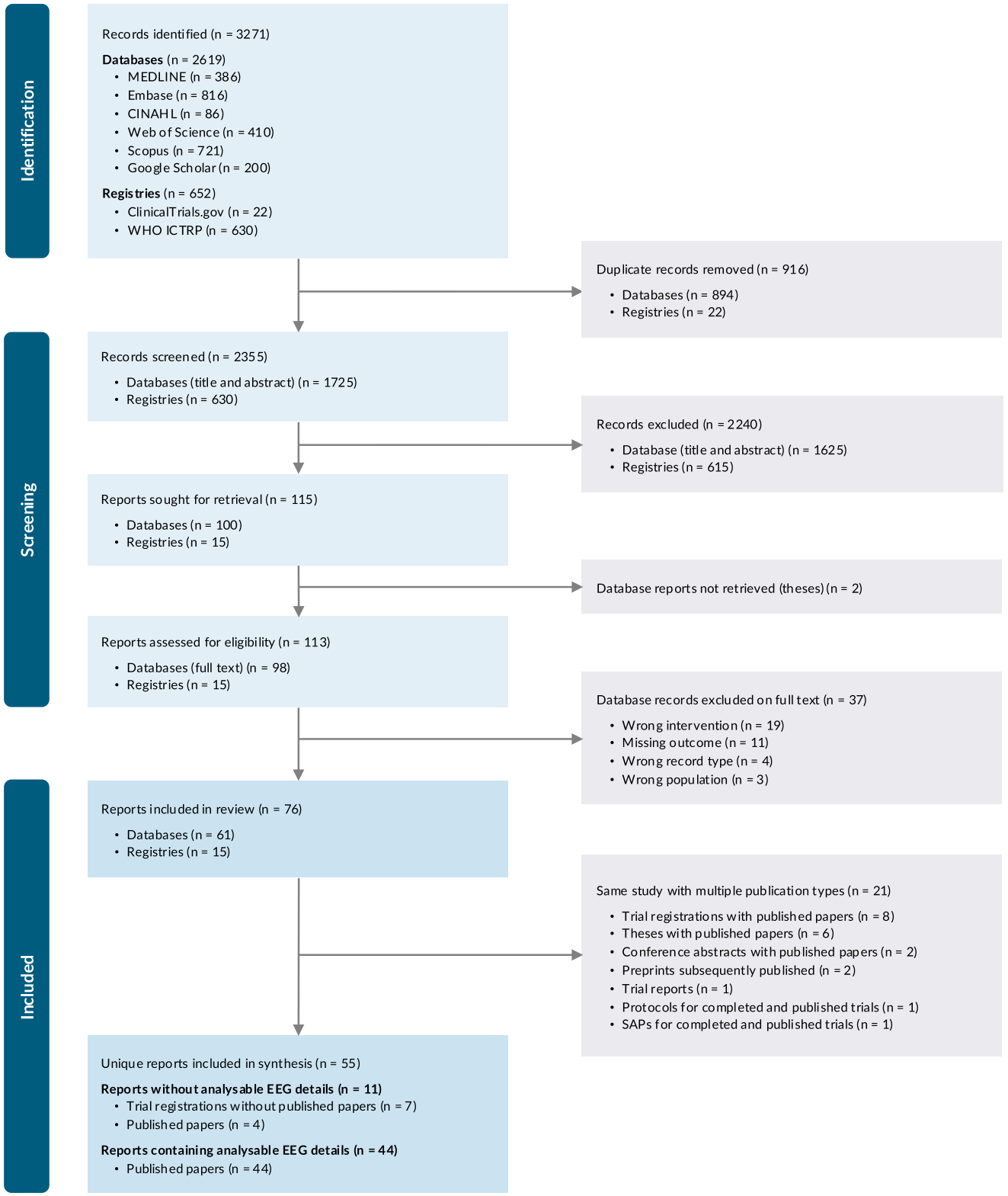

Figure 1. PRISMA flow diagram.

publications (n = 35, **Fig. 2**). We did not identify any data sets originating from South-East Asia or Africa (using WHO region definitions). The publication of research where EEG was used to study pain in neonates seems to have started in 2008 with a rate of publication of approximately 3 per year (**Fig. 2**).

3.4. Researcher coauthorship network

From the 48 studies included in the coauthorship network analysis, we identified 13 unconnected coauthorship clusters (**Fig. 3A**, Supplementary Table 6, http://links.lww.com/PR9/A400). Once this scoping review is included in the list of studies,

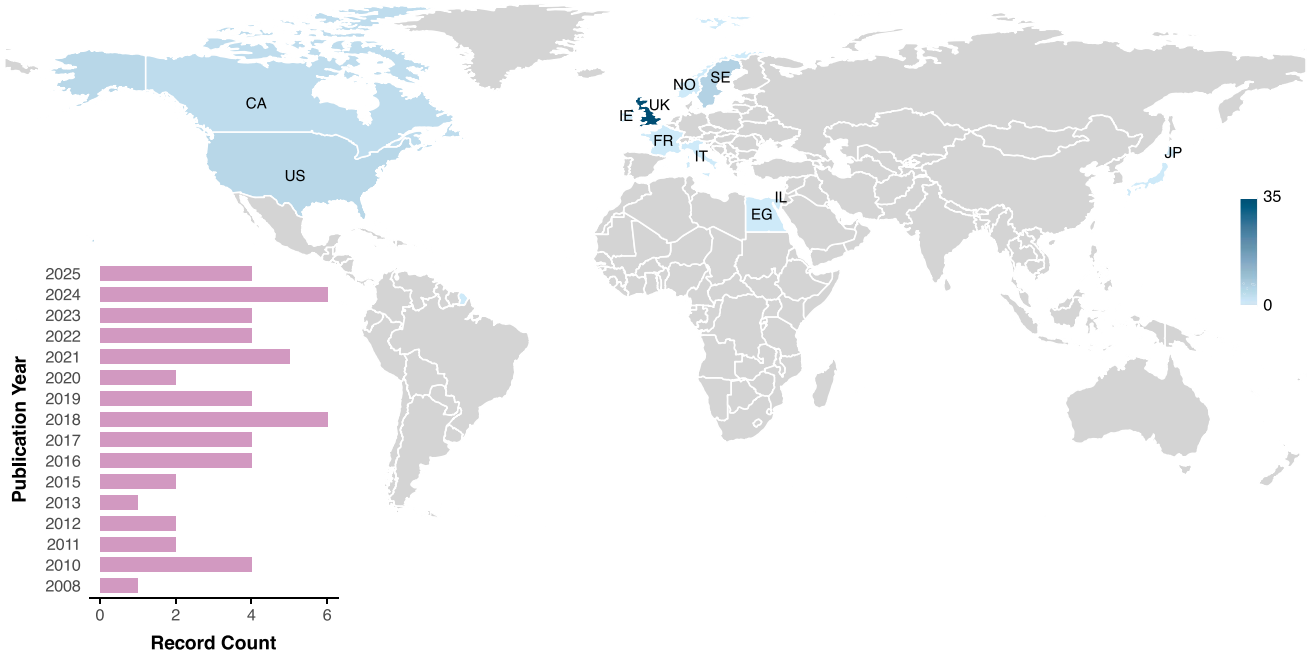

Figure 2. Country of origin of the data set and publication year of the published record. CA, Canada; EG, Egypt; FR, France; IE, Ireland; IL, Israel; IT, Italy; JP, Japan; NO, Norway; SE, Sweden; UK, United Kingdom; US, United States.

the coauthorship network connectivity increases with the number of unconnected clusters reducing to 6 (**Fig. 3B**).

3.5. Study populations

To characterize the study populations of neonates studied using EEG during painful skin-breaking procedures, we recorded the average age at birth, average age at study (PMA in weeks), and percentage of female and male neonates—**Figures 4A and B**. Taken together, the age distributions indicate that the included studies are overweighted to near-term/term-equivalent infants (median age at birth 35.2 weeks; median age at study 38.2 weeks), with earlier preterm gestations underrepresented. Sex was likewise imbalanced, with a median 12.6% higher proportion of male than female neonates across studies.

3.6. Electroencephalography

The median EEG sample size (number of neonates with EEG recordings) across studies was n = 41, with a minimum of n = 9 and a maximum of n = 268 (**Fig. 4C**). The median percentage of neonates excluded from EEG analysis due to poor EEG data quality was 4.1%, with a minimum of 0% and a maximum of 39.6% (**Fig. 4D**). Reasons for poor EEG data quality included

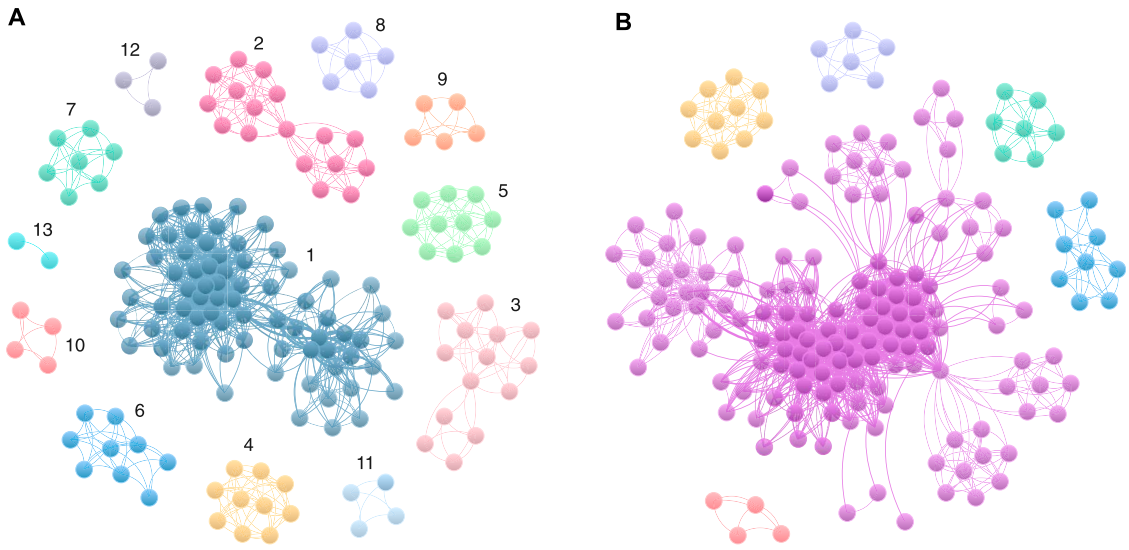

Figure 3. Researcher coauthorship networks. Nodes represent authors, edges indicate coauthorships. (A) Before this scoping review: the network comprises relatively unconnected "islands" of authors; clusters are labelled 1–13. See Supplementary Table 6, http://links.lww.com/PR9/A400 for the full author list by cluster. (B) Coauthorship network after this scoping review. Colors are consistent across panels for clusters that are unchanged; colors that appear in only one panel reflect clusters that merge into a larger connected network in the other panel.

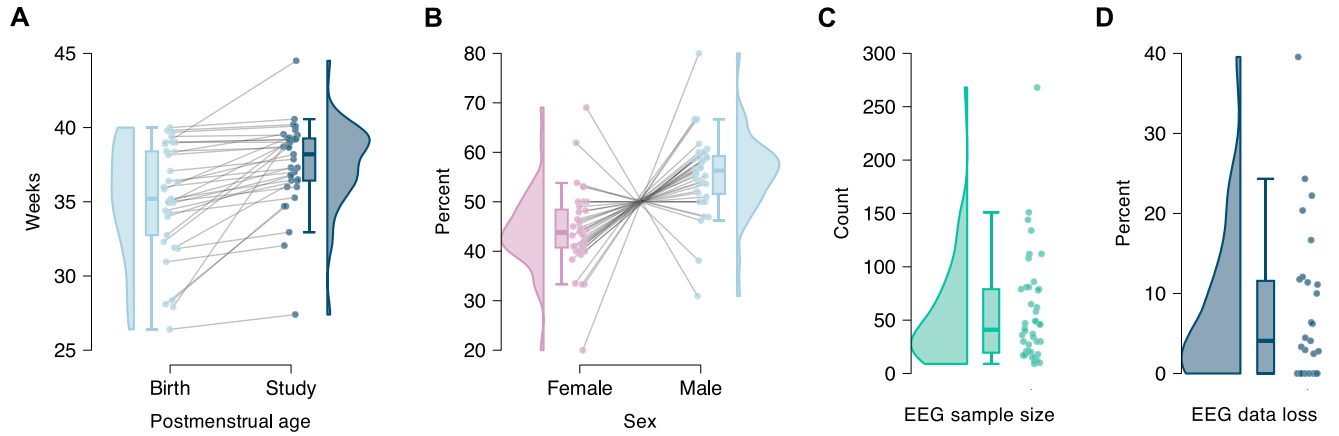

Figure 4. Study populations and EEG sample sizes. In each panel, points show study-level values, overlaid with half-violin density plots and boxplots (median and interquartile range). (A) Average postmenstrual age at birth and at study; grey lines connect paired birth and study values from the same study. (B) Sex distribution (female, male); grey lines connect paired female and male percentages within the same study. (C) EEG sample size: number of babies with EEG per study. (D) Percentage of EEG data lost due to quality issues per study.

artifacts or loss of electrode contact with the scalp. Twenty-two of 44 studies (50%) either did not report on the topic of participant loss due to EEG data quality issues or did report it, but it was unclear how many participants were specifically lost due to poor data quality. Twenty-two studies described the method by which they determined low-quality EEG data for exclusion.

We identified 3 approaches reported for identifying low data quality: objective, subjective, and mixed approaches (**Fig. 5A**). The objective approach was most often used and involved explicitly objective criteria, which in most cases was an amplitude threshold above which the epoch was classified as artifactual and rejected. The amplitude threshold used among studies varied. The subjective approach was typically described as involving "expert assessment" without further criteria provided. The lack of clear criteria that would allow reproducibility is the basis for the categorization as subjective. Five studies used a mixed-methods approach, combining objective and reproducible algorithms (an objective element) which were subsequently checked by the expert researcher (a subjective element).[6,61,69,77,84]

The use of individually placed electrodes for EEG acquisition was substantially more popular than the use of EEG caps (**Fig. 5B**). One study used novel sensors that were for combined EEG-NIRS (near-infrared spectroscopy) acquisition.[4] The frequency with which different EEG electrodes were used during acquisition also varied substantially (**Fig. 5C**). The following 8 electrodes (and number of studies) were notably the most common: Cz (36), C3 (32), C4 (32), Fz (31), T7 (30), CPz (29), T8 (29), and FCz (27).

3.7. Painful procedures and pain relief interventions

We identified 9 skin-breaking procedures used in neonatal EEG pain research (**Fig. 6A**), with heel lance being the most common procedure in 40/44 (91.0%) of studies. Some studies examined

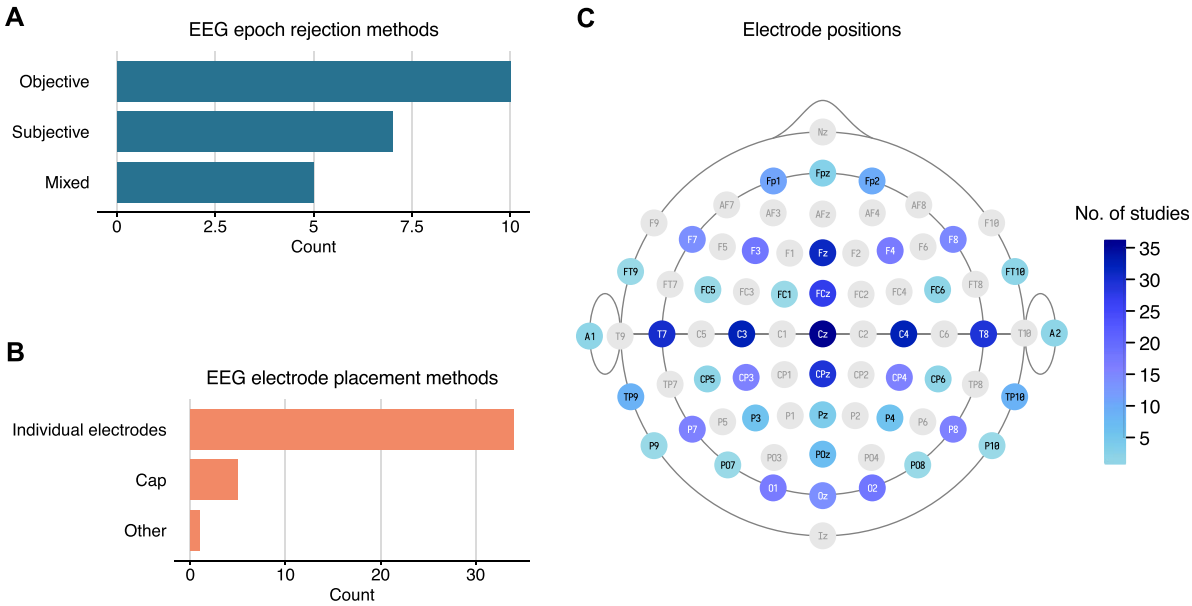

Figure 5. (A) EEG epoch rejection methods. (B) EEG electrode placement methods. (C) EEG electrode placement position frequency counts, mapped to the 10-10 system.

more than one procedure type, so the total number of procedures is larger than the number of studies.

We identified 12 interventions that were studied for their potential to provide pain relief (**Fig. 6B**). There were 7 non-pharmacological interventions: sucrose,[1,12,91] music therapy,[73] researcher-led touch-based interventions (vibration stimulation[77] and brush stroking[21,41]), parent-led touch-based interventions (stroking[47] and holding[54]), and breastfeeding.[12] There were 5 pharmacological interventions: the opioid analgesics morphine and fentanyl,[42,46,69] the nonopioid analgesic paracetamol (acetaminophen),[21] and the anesthetics sevoflurane and propofol.[18]

3.8. Nonelectroencephalography recordings

Finally, we documented other non-EEG measures of pain responses that were collected along with the EEG. These included 6 neonatal clinical pain scales, with the combination of the Premature Infant Pain Profile and its revised version together being the most common clinical pain assessment tool (**Fig. 6C**). In addition, a host of non-EEG recordings were identified, including hemodynamic brain responses (ie, NIRS), behavioral, cardiovascular, respiratory, and hormonal responses (**Fig. 6D**).

4. Discussion

This scoping review is the first stage in an IPD meta-analysis, with the findings from this review guiding the next stages of the project.[9] This scoping review identified 55 unique publications using EEG to assess acute pain in neonates, with 164 global researchers having published articles using EEG for this purpose. Electroencephalography has been commonly used during acute painful procedures in neonates, with studies being conducted in 11 countries since 2008. Electroencephalography has often been acquired alongside other pain-relevant recordings, which will facilitate assessments of the relationships that pain-related EEG activity may have with other pain-related signals.

We identified 13 clusters of researchers publishing in this area, with limited overlap between "islands" of authors. To consolidate and connect researchers who have investigated neonatal pain using EEG, we invited authors of the relevant literature to contribute to and coauthor this review and to facilitate future collaborations in this developing field. While EEG studies span multiple countries, most originate from Europe and the Americas, highlighting gaps in global neonatal pain research. Regional differences in neonatal care, cultural perceptions of pain, and technological access influence this disparity. Limited participation of researchers from South America, Africa, and Asia in this review limits the generalizability of the findings. This is likely due to the equipment being expensive to purchase, requires expert personnel to perform the studies and interpret the results, and is labor-intensive to maintain. Collaborative efforts must be made to ensure that future research is inclusive of diverse global populations, which will enrich the understanding and utility of EEG in neonatal pain assessment.

The EEG measures used in the studies identified in this review offer objective neurophysiological metrics that could be used to augment traditional neonatal pain scales. However, technical demands and the need for specialized personnel hinder its routine clinical use. The development of EEG-integrated monitoring systems with flexible or wireless electrodes could help bridge this gap. Developing automated systems capable of real-time EEG analysis could also help make EEG a more practical tool

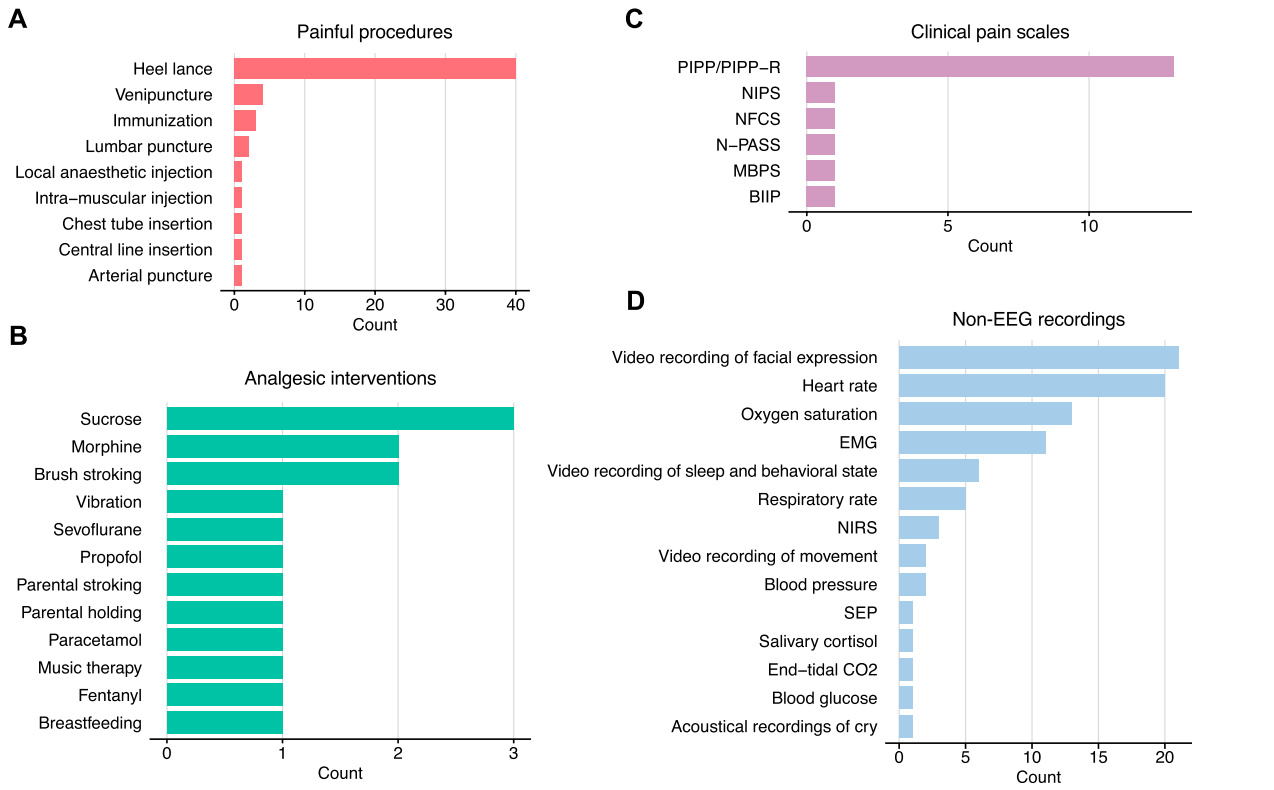

Figure 6. (A) Painful (ie, skin-breaking) procedures. (B) Analgesic interventions. (C) Clinical pain scales. (D) Non-EEG recordings. BIIP, Behavioral Indicators of Infant Pain; CO_2, carbon dioxide; EMG, electromyography; MBPS, Modified Behavioral Pain Scale; NIPS, Neonatal Infant Pain Scale; NFCS, Neonatal Facial Coding System; NIRS, near-infrared spectroscopy; N-PASS, Neonatal Pain, Agitation, and Sedation Scale; PIPP(-R), Premature Infant Pain Profile (Revised); SEP, somatosensory evoked potential.

for routine bedside pain assessment. In addition, EEG biomarkers of neonatal pain could be used in nonroutine, well-structured, high technology contexts such as clinical trials either as a stand-alone outcome or as one item in a multidimensional pain scale assessment.[82,83] The technical and logistical needs, as well as the acceptability of the technique, will depend on the context of use. Before an EEG metric will be broadly acceptable, either as an item to be integrated into traditional neonatal pain scales or as a stand-alone outcome, basic measurements of reliability, validity, and interpretability will need to be established for any EEG metric.[9,25] In addition, optimal methods for EEG monitoring and electrode placement in neonates are not readily available, especially for longer-term monitoring, highlighting the need for standardized protocols.[59]

Regardless of how EEG biomarkers of acute neonatal pain are implemented, integrated, or scaled up (eg, wired or wireless individual electrodes or caps; integrated with existing pain-relevant indicators and pain scales or used as stand-alone outcomes; scaled up for routine clinical use or large-scale clinical trials), data quality issues must be considered carefully. In this review, we identified that loss of participants from analysis due to EEG data quality seems to be a significant issue for some studies. The median data loss was 3.3%, which is consistent with similar numbers reported with the use of nonpainful stimuli in this age range,[94,102] suggesting the issue is likely to be related to the neonatal population rather than the painful procedure. Furthermore, the methods involved in assessing EEG data quality were not always clearly presented and often left undescribed, thus limiting the reproducibility of this step in the analysis process. These reproducibility and data loss issues pose a challenge to the field. Loss of data will reduce precision and may introduce selection bias (eg, neonates with more movement-related artifacts may be disproportionately excluded from analysis)[48,49] or bias by indication (ie, certain types of neonates requiring a specific type of painful procedure), and the resulting lack of reproducibility will be a barrier to general uptake. Addressing these limitations requires a concerted effort to develop better technologies and standardized protocols. Innovations in EEG hardware (eg, wireless electrodes) could reduce movement-related artifacts, and standardized protocols with clear data quality criteria that combine objective algorithms with human verification for data quality control could improve reproducibility and reduce risk of bias. For research studies including EEG assessments, all these complexities will require careful specification of analytic methods in statistical analysis plans, which include sensitivity tests and appropriate methods to assess and handle missing data.[29]

We identified multiple distinct research groups with relatively large data sets, demonstrating the existence of sufficient EEG data recorded in neonates during acute skin-breaking procedures to conduct an IPD meta-analysis designed to assess the reliability, validity, and interpretability of a specific EEG outcome measure.[9] Compared with standard aggregate data meta-analysis, an IPD meta-analysis can potentially provide substantial improvements to the extent and quality of data available, by including both reported and unreported data and addressing data completeness and quality issues directly with original investigators.[98] This approach could increase sample size, statistical power, and generalizability.[78] Collaborating with original investigators in an IPD meta-analysis study provides deeper insights and fosters a network for sharing neonatal EEG data, enabling novel research opportunities. Other research groups have already begun generously sharing their neonatal pain IPD data sets,[55] which has created new research opportunities and findings.[96,100] Through our IPD meta-analysis project, we plan to continue expanding and advancing the data sharing efforts to help transform the field of neonatal pain research.[9]

Pooling of data across studies will be limited by heterogeneity and inconsistencies in data collection methodologies. In this review, we identified that electrode coverage of the scalp varied considerably, with central electrodes being the most recorded. For analyses that require central electrodes, such as the specific Cz-Fz channel biomarker that we are assessing in our IPD meta-analysis, significant value will be gained from pooling these data sets. However, for research questions that require recordings from brain regions not covered by certain electrodes, or for analytic methods that require relatively high electrode numbers, use of existing data sets might be more limited. For example, microstate analysis is becoming increasingly popular in neonatal EEG analysis,[14,66,80] using information that can be obtained from a full-scalp electrode array to detect and analyze signals otherwise inaccessible to traditional event-related potential analysis, such as signals from the subcortical loci used for pain processing. Pooling existing data sets with limited and inconsistent scalp coverage may cause more challenges to implementing microstate analysis than event-related potential analysis. However, highlighting challenges is often a necessary first step in overcoming them, and methodological progress for complex nonevent-related potential analytic approaches would likely accelerate if researchers had access to these pooled data sets.

5. Conclusion

The development of more accurate and reproducible pain measures for neonates is urgently needed. This scoping review is an initial component of a larger project addressing this issue by taking the necessary steps to establish a pain-related EEG biomarker to help create novel brain-based clinical pain measures. This review identified 55 studies that used EEG-based measures to help quantify changes in noxious stimulation-evoked brain activity in neonates. Identifying this substantial body of literature through a scoping review raises awareness of the value that neonatal EEG studies can bring to better understand the occurrence and treatment of neonatal pain. There is great value in bringing these data sets together as these difficult-to-collect data have tremendous value beyond the single studies for which the data were initially collected. Future collaborative efforts will further develop the data acquisition and analytic skills that are needed to further progress this field. This work forms the groundwork for a future IPD meta-analysis where we can bring this community together to share and store data using the infrastructure within the Critical-Path Institute's Rare Disease Cures Accelerator-Data and Analytics Platform.[7] This is a valuable initiative funded by the US Food and Drug Administration that provides a centralized and standardized data analytics infrastructure to ensure safe and secure data storage that meets FAIR (Findability, Accessibility, Interoperability, and Reusability) data principles.[52,108] By bringing this community together, great advances are possible in the use of brain-derived approaches to better understand how afferent noxious input is processed by the immature neonatal brain and ultimately how to modify these signals to improve the experiences of newborn babies.

Disclosures

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Author contributions statement: P.Y.G. designed the methodology, developed the software, performed the formal analyses, conducted the investigation, curated the data, drafted the initial manuscript, and prepared the visualizations. L.B. conceptualized and designed the study, developed the software, performed the formal analyses, curated the data, drafted the initial manuscript, prepared the visualizations, provided supervision, and coordinated and administered the project. M.M.C. validated the results, prepared the visualizations, and critically reviewed and revised the manuscript. M.v.d.V., S.I., V.M., K.J.S.A., C.B.B., C.C., M.R.D., G.D., V.F., B.G., C.H., P.K., N.L.M., R.C.M., S.M., S.N., E.N., S.T., and S.W. conducted investigation through the provision of primary study data, validated the accuracy of the data extraction, and contributed to interpretation through critical review and revision of the manuscript for important intellectual content. K.A., J.M.D., M.A.T., R.M.W., E.D., J.P.S., A.B., J.v.d.A., and A.N.M. conceptualized and designed the study, and critically reviewed and revised the manuscript. K.S. conceptualized and designed the study, secured funding, coordinated and administered the project, and critically reviewed and revised the manuscript. R.S. conceptualized and designed the study, provided resources, supervised the work, coordinated and administered the project, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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