ELECTROENCEPHALOGRAPHY MONITORING IN THE CRITICALLY ILL

Towards a More Efficient and Effective Monitoring Strategy

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June 2023

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Student Number: 4453778
June 19, 2023

Thesis in partial fulfilment of the requirements for the joint degree of

Master of Science

in Technical Medicine

Leiden University; Delft University of Technology; Erasmus University Rotterdam

Master thesis project (TM30004; 35 ECTS)
Department of Neurology - Clinical Neurophysiology
Erasmus MC
Dec 2022 – July 2023

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Preface

When I was in my third year of pre-university education and was way too late with arranging my “snuffelstage”, my aunt came to the rescue. Eventually, I got the opportunity to experience the combination of medicine and technology for the first time at her job as a vascular technician. Shortly after, I discovered the existence of a new program in Delft that immediately sparked my enthusiasm. Now, several years later - after a slight detour of studying Architecture when the odds weren’t in my favour - this story concludes with writing this page of my Master’s thesis in Technical Medicine. During my first clinical internship in early 2021, I had the opportunity to get acquainted with neurophysiological research for the first time. Throughout subsequent internships, my fascination for the most mysterious organ in our body, the brain, continued to grow. Additionally, I became drawn to the acute care environment of the intensive care unit. Throughout the past year, I have been incredibly fortunate to merge these interests in my graduation project. During the course of this project, I received assistance from a diverse group of individuals who provided invaluable support and guidance.

The first person I would like to express my gratitude to is my medical and daily supervisor, Robert. Thank you for your endless enthusiasm, valuable insights, and dedication to the project. Perhaps even more importantly, thank you for helping me develop various soft skills and organising every aspect of the project with me. I thoroughly enjoyed the way we could contemplate every little detail together. To my technical supervisor Mark, thank you for your critical perspective and insights from outside of the hospital. Your input has made me reflect on the connection between technology, research, and clinical practice multiple times. I am incredibly excited and grateful for the opportunity to keep working with the both of you for the upcoming years.

There are several other individuals who have contributed to the successful completion of this project. When I started this project 7 months ago, I was completely clueless on the conduction of qualitative research, and without the advice and guidance of Rachel I wouldn’t have known where to start. Judith, thank you for providing your carefully maintained database of all patients suffering from postanoxic encephalopathy in our ICU. Furthermore, I would like to express my gratitude to all the physicians, residents, and technicians of the Clinical Neurophysiology department for enabling me to gain clinical experience and for the enjoyable and insightful discussions we had regarding my project. However, I did not only get input from the clinical neurophysiology department. Mathieu, thank you for your valuable input from an ICU perspective. Your insights and suggestions have been greatly appreciated.

To my family and friends, thank you for all the support, pep talks, moments of distraction, and shared study sessions over the past eight years. Your presence and encouragement have meant the world to me. To the “kantoortuin crew” at Nf-3, I will miss our countless coffee- and lunch breaks, it was a pleasure. A special thank you goes to Emma for the fun collaborations throughout our studies, the relentless cheerleading whenever I felt overwhelmed, and for your enthusiastic and valuable ideas for my project. I am eagerly looking forward to our continued collaboration in the years to come. To Mar, after all these years of lending your ears to my project rants, you’ve practically earned the honorary title of Technical Physician. The most heartfelt thank you goes out to you for your endless support, love, and for managing nearly every aspect of my life so I could focus on writing this thesis.

Finally, I would like to extend my gratitude to myself, for reaching a point where I can genuinely take pride in this work. I am filled with excitement and curiosity about what the future holds.

Marit Verboom
June 2023

Summary

Critically ill patients in the Intensive Care Unit (ICU) are often comatose and thoroughly monitored. Neurological complications occur in up to 20% of these patients. Therefore, monitoring of the brain, which can be performed using electroencephalography (EEG), has the potential to significantly impact the outcomes of patients at the ICU. Despite the potential of EEG as a noninvasive method for monitoring the neurological status of critically ill patients, the labor-intensive and complex nature of its application and assessment has hindered widespread implementation. Therefore, the aim of this thesis was to identify the logistical and technical prerequisites for efficient and effective neuromonitoring using EEG in the ICU.

Chapter 1 provides an overview of neuromonitoring techniques in the critically ill patient. It delves into the neurophysiological background of the EEG, the techniques used for applying the EEG electrodes, and the EEG assessment.

In **Chapter 2** we present a qualitative study on the optimal conditions for EEG monitoring in the ICU. Through 12 individual and 2 focus group interviews with employees from different departments within and outside of the hospital, the current workflow regarding neuromonitoring in the ICU is identified. Additionally, we evaluate the barriers and facilitators for change in this monitoring process through the Consolidated Framework for Implementation Research (CFIR). Factors such as motivation and willingness to change serve as facilitators, while a lack of interdepartmental communication and the high workload for various healthcare professionals involved can be significant barriers.

The qualitative research reveals that the largest group monitored using EEG in the ICU consists of patients suffering from postanoxic encephalopathy, which can be a complication of a cardiac arrest. Therefore, in **Chapter 3**, we examine the technical requirements for optimal EEG monitoring. Specifically, we focus on the necessary number of EEG electrodes for reliable automatic classification of the EEG background pattern in postanoxic encephalopathy. By training an Random Forest (RF) classifier with input from 12, 10, 8, 6, and 4 EEG electrodes, we develop a model with a micro-averaged One-vs-Rest (OvR) Area Under the Curve - Receiver Operating Characteristics (AUC-ROC) value of 0.923, 0.924, 0.924, 0.925, and 0.923 (p-value: 0.279) for the different numbers of electrodes respectively. The constant performance of the model suggests that a reduced number of electrodes may be sufficient for monitoring this patient group, potentially reducing the workload for EEG technicians. Automatic assessment of the EEG can also contribute to a decreased workload for clinical neurophysiologists.

In **Chapter 4** we provide the conclusions and future perspectives of this thesis. We have demonstrated the potential for change in the EEG monitoring workflow at the ICU of the Erasmus MC, indicating that there is an opportunity to work towards more effective and efficient neuromonitoring. Future research should focus on a broader range of logistical and technical prerequisites - including effective interdepartmental collaboration and which EEG equipment to use - thereby creating opportunities to improve treatment and outcomes of critically ill patients.

Abbreviations

A(N)IOS	Arts (niet) In Opleiding tot Specialist
ACNS	American Clinical Neurophysiology Society
aEEG	amplitude-integrated electroencephalography
AI	Artificial Intelligence
ANOVA	Analysis of Variance
ApEn	Approximate Entropy
AUC-ROC	Area Under the Curve - Receiver Operating Characteristics
BCorrD	Bivariate Correlation Directed
BIDS-EEG	Brain Imaging Data Structure for EEG
BS	Burst Suppression
BSR	Burst Suppression Ratio
CA	Cardiac Arrest
cEEG	continuous electroencephalography
CFIR	Consolidated Framework for Implementation Research
CN	Clinical Neurophysiology
CT	Computed Tomography
DCI	Delayed Cerebral Ischemia
ECG	electrocardiogram
EEG	electroencephalography
EMC	Erasmus Medical Center Rotterdam
EMG	Electromyogram
EPSP	Excitatory Postsynaptic Potential
ERP	Evoked Response Potentials
ESICM	European Society of Intensive Care Medicine
ESR	EEG Silence Ratio
FFT	Fast Fourier Transform
FIR	Finite Impulse Response
GABA	Gamma-Aminobutyric Acid
GCS	Glasgow Coma Scale
GPD	Generalised Periodic Discharges
ICA	Independent Component Analysis
ICH	Intracerebral Hemorrhage
ICP	Intracranial Pressure
ICU	Intensive Care Unit
IHCA	In Hospital Cardiac Arrest
IPSP	Inhibitory Postsynaptic Potential
ML	Machine Learning
MRI	Magnetic Resonance Imaging
NCSE	Non Convulsive Status Epilepticus
NCSz	Non Convulsive Seizures
NMC Lab	Delft Laboratory for NeuroMuscular Control
OHCA	Out of Hospital Cardiac Arrest
OvR	One-vs-Rest
PA	Physician Assistant
PICU	Pediatric Intensive Care Unit

PLI	Phase Lag Index
PSD	Power Spectral Density
qEEG	quantitative electroencephalography
RF	Random Forest
ROC	Receiver Operating Characteristic
SAH	Subarachnoid Hemorrhage
SE	Status Epilepticus
SEF	Spectral Edge Frequency
SEF90	Spectral Edge Frequency at 90% of the power spectrum
SNR	Signal to Noise Ratio
SpEn	Spectral Entropy
T24	24 hours after cardiac arrest
TBI	Traumatic Brain Injury
TsEn	Tsallis Entropy
TTM	Targeted Temperature Management
VA-ECMO	Veno-Arterial ExtraCorporeal Membrane Oxygenation

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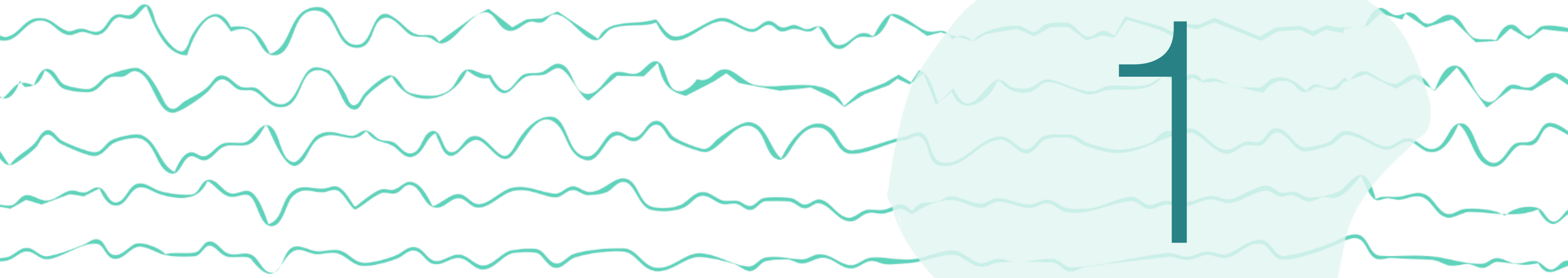

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BACKGROUND

1.1 Neuromonitoring in the Intensive Care Unit

In the Intensive Care Unit (ICU), most patients are comatose. The organs of critically ill patients are susceptible to damage and deterioration, and are therefore thoroughly monitored. [1] Part of the patients admitted to the ICU suffer from primary brain injury, while all patients face the potential risk of experiencing acute or secondary brain injury during their admission, as neurological complications occur in up to 20% of critically ill patients. [2, 3] Hence, it is imperative to thoroughly monitor the brain alongside the monitoring of all other organs.

1.1.1 Acute brain injury

Acute brain injury can arise from various causes in the critically ill patient. Strokes caused by disrupted blood flow to the brain, Traumatic Brain Injury (TBI) resulting from head trauma, and hypoxic-ischemic injury due to oxygen deprivation are common culprits. Additionally, infections like meningitis or encephalitis, Intracerebral Hemorrhage (ICH) and Subarachnoid Hemorrhage (SAH) from ruptured aneurysms or head trauma, metabolic disturbances, and seizures can all contribute to acute brain injury in the ICU. [4, 5] The cascade of events triggered by a primary brain injury, either upon admission or as a neurological complication, can result in the occurrence of secondary brain injury. If not treated in a timely manner, this secondary injury can escalate and contribute to the progression of neurodegeneration (Figure 1.1). [6, 7] Adequate neuromonitoring is of great importance in this process, as it could facilitate the timely detection and intervention of critical changes in cerebral physiology. Early recognition and targeted interventions can help mitigate the secondary cerebral complications that may benefit from treatment, thereby reducing the progression towards neurodegeneration. Therefore, integrating comprehensive neuromonitoring into the management of critically ill patients is essential to optimise patient outcomes and minimise long-term neurological consequences. [4, 7]

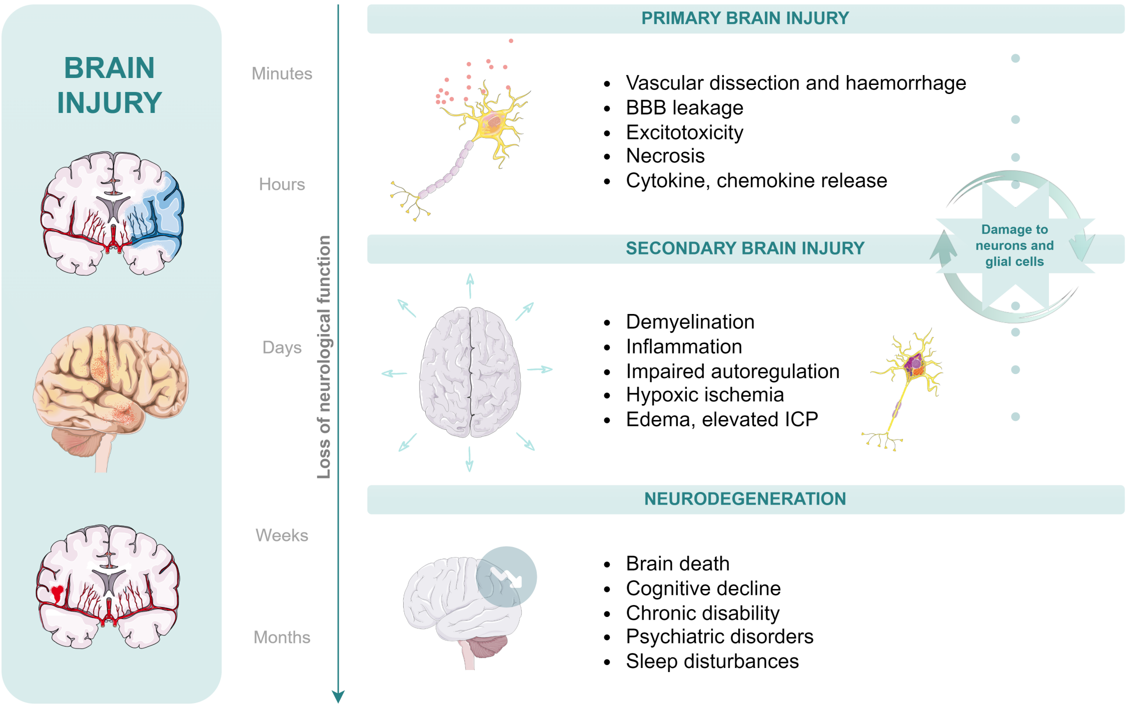

Figure 1.1: Part of neuropathological cascades after acute brain injury. The primary brain damage occurs within brief time intervals after the initial brain injury. This initial damage triggers a series of chemical cascades that ultimately lead to the onset of secondary damage (which can in turn increase the susceptibility to primary brain injury). Although the secondary damage extends over hours to days, it can contribute, in conjunction with repeated exposure to traumatic events, to the initiation of various neurodegenerative processes associated with cognitive and behavioral impairments. Parts of the figure were drawn by using pictures from Servier Medical Art. Servier Medical Art by Servier is licensed under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/).

1.1.2 Neurological examination

Bedside neurological exam, including the is the most important assessment to evaluate the level of consciousness and neurological functioning in the ICU. The GCS is used to evaluate three key components: eye-opening (E), motor- (M), and verbal- (V) response. [8] After assessing each of these components, the scores for E, M and V are added together to obtain the overall GCS score, which ranges from 3 to 15. A higher score indicates a higher level of consciousness and neurological function. All ICU patients are examined using the GCS several times a day. However, the score does not allow for continuous monitoring and relies on the interpretation of the examiner, introducing subjectivity. [9] Furthermore, it assesses only a limited set of parameters and may not capture all aspects of neurological function, sedation can interfere with accurate scoring, and subtle changes in neurological function may go undetected. Despite these limitations, the GCS remains widely used as a standardised tool for initial neurological assessment in the ICU. Augmenting the GCS with additional diagnostic modalities could overcome its limitations and obtain a more accurate assessment of the patient's neurological status.

1.1.3 Monitoring modalities

A wide array of invasive and noninvasive methods exist for neuromonitoring in critical ill patients (Table 1.1). These modalities offer potential targets for therapeutic interventions, allowing for the prevention and treatment of secondary brain injury. [10] Among the most commonly used modalities in the ICU are Computed Tomography (CT)/Magnetic Resonance Imaging (MRI), Intracranial Pressure (ICP) cathether and electroencephalography (EEG). [5, 10, 11] CT and MRI provide valuable structural imaging to identify brain lesions, hemorrhages, and masses. Their main advantage lies in their ability to visualise detailed anatomical information. However, these modalities are not suitable for continuous monitoring and may require patient transportation, limiting their use in unstable patients. Another type of monitoring that is regularly used in the ICU is ICP monitoring using an intracranial catheter, to manage cerebral perfusion. [12] Nonetheless, invasive ICP monitoring carries risks such as infection and hemorrhage. Lastly, EEG can be used to record the electrical activity of the brain, aiding in the detection of seizures and assessing the overall brain function and is recommended in a variety of ICU patients. [13]

Table 1.1: Frequently used neuromonitoring modalities in the Intensive Care Unit (ICU) and their (dis)advantages (presented in alphabetical order). [7] CT: Computed Tomography. BIS: Bisprectral index. EEG: Electroencephalography. ICP: IntraCranial Pressure. MRI: Magnetic Resonance Imaging. NIRS: Near-Infrared Spectroscopy. TCD: TransCranial Doppler. CBF: Cerebral Blood Flow.

Modality	Advantages	Disadvantages
CT	Strucutral evaluation of brain injury	Non-continuous Radiation load Limited availability
BIS	Non-invasive Continuous Easy to interpret	Limited spatial resolution No raw data available
EEG	Non-invasive Continuous Overal brain functioning	Complex interpretation Complex attachment
ICP	Direct ICP measurement Continuous	Invasive Not sensitive for compensatory mechanisms Risk of hemorrhage, infection
MRI	High spatial resolution Non-invasive	Non-continuous ICU equipment non-compatible Not directly available at ICU
NIRS	Non-invasive Continuous	Limited accuracy
TCD	Bedside Non-invasive assessment of CBF	Complex interpretation Correct measurement requires training

1.2 Electroencephalography

The EEG is a non-invasive tool, which involves the application of electrodes to the scalp of a patient to measure electrical activity, and allows for continuous monitoring of the brain. The American Clinical Neurophysiology Society (ACNS) recommends continuous electroencephalography (cEEG) in the ICU for several indications, namely the diagnosis of Non Convulsive Seizures (NCSz) and Status Epilepticus (SE), the assessment of efficacy of therapy for seizures and SE, monitoring of sedation and high-dose suppressive therapy, the identification of cerebral ischemia, and the neurological prognosis in several diseases. [14]

1.2.1 Neurophysiology and the EEG signal

To comprehend the signals captured by EEG, it is crucial to have a fundamental grasp of neurophysiology. The function of the brain depends of the interaction of single cells (neurons) in complex networks. Information is passed through these networks using electrical signals, generated by neurons. At the synapses, the contact points between neurons, these electrical action potentials are "translated" into chemical signals, the neurotransmitters. Among the most prominent neurotransmitters that play a role in the transmission of the electrical activity of the brain are the excitatory neurotransmitter glutamate, and the inhibitory neurotransmitter Gamma-Aminobutyric Acid (GABA). [15] Glutamate causes an Excitatory Postsynaptic Potential (EPSP). Subsequently the cell will depolarise: the Na$^+$/K$^+$ channels open, Na$^+$ flushes into the cell, and the membrane potential (with a resting stage of approximately -70mV) will turn positive (around +20mV). Outside of the cell however, the depolarisation of the neuron will lead to a relatively negative charge. In contrast, GABA causes an Inhibitory Postsynaptic Potential (IPSP) that will lead to hyperpolarisation of the cell. K$^+$ moves out of the cell and the membrane potential of the cell will turn more negative (approximately -100mV). Therefore, outside of the cell there will be a relatively positive charge.

Using EEG, it is possible to directly measure the electrical activity of the brain. The signals that are measured by EEG electrodes reflect the postsynaptic extracellular potentials of neurons in the cortex of the brain (Figure 1.2). The electrical activity of a single neuron is far too small to be detected on a scalp EEG. Thus, what is reflected on the EEG is a summation of synchronised activity of a group of

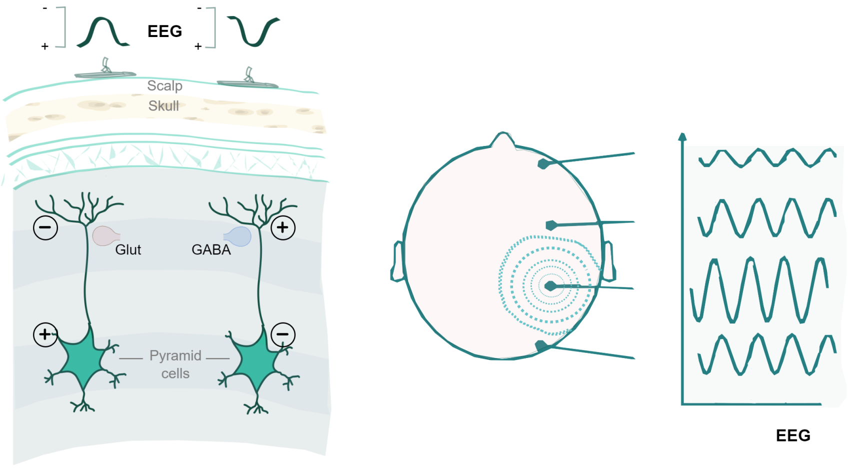

Figure 1.2: Electrophysiology of the electroencephalography (EEG) signal. Illustration depicting the generation of EEG signals through the interaction of neurons (pyramidal cells) in the cortex, glutamate, and GABA. Excitatory glutamate (Glut) causes the outside of pyramidal cells to become negative, while inhibitory GABA leads to a positive charge. These cellular dynamics result in a measured EEG signal, where positive activity induces downward waves on the EEG trace. As the EEG electrodes move further away from the source of neural activity, the amplitude of the EEG signal decreases. Adapted from Mecarelli (2019) [16].

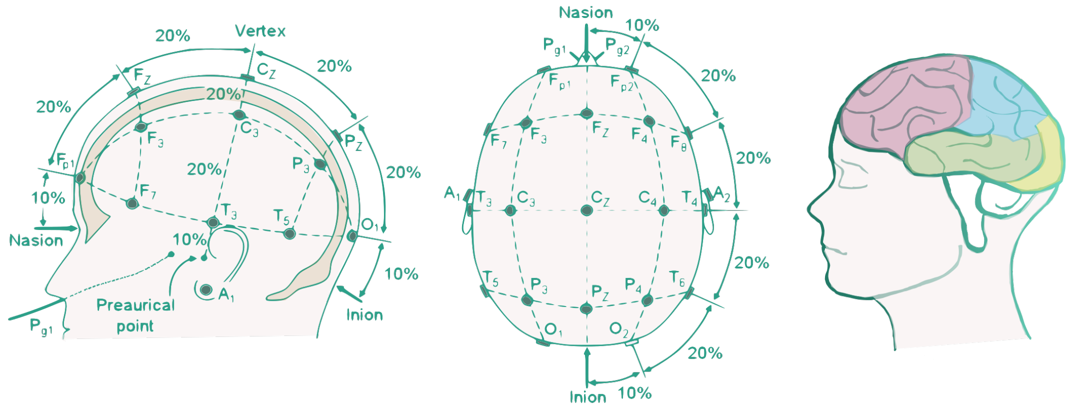

Figure 1.3: The international 10-20 system for EEG electrode placement. This standardised system divides the scalp into distinct regions, with electrodes positioned at percentages of 10-20% the distance between anatomical landmarks. F: frontal (pink). T: temporal (green). P: parietal (blue). O: Occipital (yellow). C: central. Adapted from Shriram et al. (2012) [19]

neurons. [17] EEG electrodes measure the extracellular potentials at the surface of the cortex, which are then translated into the waveforms displayed on the EEG as voltages by calculating the charge differences between two electrodes. Counter-intuitively, positive values are displayed as downward waves, and negative values are displayed as upward waves. Charge differences are calculated between two electrodes in a montage. A montage is the specific arrangement of different channels, where a channel is the difference between a pair of electrodes. Different montages can be used for e.g. the localisation of the maximal electrical activity. Montages that are used most frequently for clinical EEG recordings are bipolar and referential montages. [18] Bipolar montages display channels with electrode pairs, whereas referential montages consists of e.g. one common reference electrode or the average of all electrodes as reference electrode.

1.2.2 Electrode application

The process of the application of EEG electrodes can be time-consuming, as an EEG technicians should carefully preprare the scalp of the patient, apply conductive gel/paste and attach the electrodes one by one at exact locations. The goal of this approach is to minimise the impedance of the electrodes to increase the Signal to Noise Ratio (SNR). The application process, typically performed using the 10-20 system, may take up to 60 minutes depending on factors such as the number of electrodes used, hair type, skin condition, and sweat on the patient's scalp.

The international 10-20 system provides a systematic approach to accurately and consistently apply EEG electrodes on the scalp and is based on the relative distances between anatomical landmarks on the head. The landmarks that are typically used include the nasion (the bridge of the nose), the inion (the bony prominence at the base of the skull), and the preaurical point of both ears. [20, 21] Using this system, the skull is split into segments of 10% or 20% of the total circumference of the skull and electrodes are attached accordingly (Figure 1.3). EEG electrodes are denoted by a letter and a number. Every letter corresponds to the region of the brain where the electrode is placed (F: frontal, C: central, P: parietal, O: occipital), and the numbers correspond to the side of the head. The odd-numbered electrodes are located on the left side of the head, while the even-numbered electrodes are on the right side. Central midline electrodes are denoted by a "z". By using this system, it is ensured that the electrode placements are proportional to the shape and size of the skull. Therefore it allows for a replicable and reliable EEG recording. Due to the development of digital-EEG and the introduction of high-density EEG and source localisation methods, an expansion of electrode arrays was required. As a result, a modification involving the use of the 10-10 system was proposed, which ensures greater electrode coverage and allows for more accurate localisation of brain activity. Although the 10-10 combinatorial nomenclature is not extensively employed in ICU settings at present, there can be occasional confusion with its terminology. Specifically, certain electrode definitions at equivalent positions might get mixed up. Examples of such common mix-ups include T3 being equivalent to T7, T4 to T8, T5 to P7, and T6 to P8. [22]

1.2.3 EEG assessment

The analysis of EEG recordings traditionally is performed during a time- and labour-intensive process by a trained clinical neurophysiologist. The ACNS has established a guideline for characterising EEG findings in critical care settings. Adhering to this standardised terminology enhances communication among healthcare professionals and aids in the identification of specific EEG patterns associated with various neurological conditions or abnormalities. [23] Over the recent years, the computational analysis of EEG signals (also known as quantitative electroencephalography (qEEG)) has gained interest. [24] The quantitative analysis of EEG allows for quick analysis of large amounts of data, reducing the time- and labour-intensive process of EEG assessment. Using mathematical algorithms, EEG features like the amplitude and frequencies can be calculated. Although several commercially available packages are on the market, they usually are not specifically designed for usage at the ICU, and therefore are not widely used in clinical practice yet. [25]

Artefacts

EEG signals are extremely sensitive to artefacts. Every phenomenon on the EEG that is not generated by the brain itself, can be considered an artefact. Awareness of possible artefacts is of great importance when analysing the EEG. For the visual assessment, this means that the assessor should be trained and able to recognise all artefacts. Although video-EEG helps to distinguish artefacts from neurophysiological signals, this remains a challenge. EEG artefacts can be of exogenous (outside of the body, caused by the acquisition system or external equipment) and endogenous (within the body, physiological) origin. [16] In the ICU environment, the presence of various equipment often leads to the occurrence of exogenous artefacts. The most frequent exogenous artefact is the power supply component of 50 Hz, caused by the excessive amount of electronic equipment in the ICU. This is followed by artefacts of poor electrode contact to the scalp due to poor attachment and movement of patients during patient care. Additionally, sweatbridges can be formed when sweat of the patient connects two electrodes causing direct electrical conduction, which can influence signal quality. Endogenous artefacts include eye movement, the electrocardiogram (ECG), Electromyogram (EMG), body movement due to respiration, tremor or myoclonus.

1.3 Thesis objective

Despite the potential of EEG as a noninvasive method for monitoring the neurological status of critically ill patients, its labor-intensive nature in application and assessment has hindered widespread implementation. While our hospital, the Erasmus Medical Center Rotterdam (EMC), primarily utilises EEG monitoring at the ICU for the prognostication in postanoxic encephalopathy, and the diagnosis and monitoring of Non Convulsive Status Epilepticus (NCSE), recent studies suggest broader applications. [26] Thus, the objective of this thesis is to identify the optimal conditions for efficient and effective neuromonitoring using EEG in the ICU. What are the minimal logistical requirements? What resources can we count on in our hospital, and what aspects require additional attention? What is minimally needed for technically accurate EEG signals with preserved SNR and sufficient information? To address part of these questions, subgoals are:

1. To evaluate the current workflow and identify pitfalls, wishes and opportunities for improvement in the current neuromonitoring workflow at the ICU of the EMC using EEG (**Chapter 2**)
2. To determine the minimum amount of required EEG electrodes for automatic EEG background pattern scoring in postanoxic encephalopathy using a Machine Learning approach (**Chapter 3**)

The findings of this thesis could be used for future implementation of new EEG equipment at the ICU to reduce labour intensiveness, provide better patient specific healthcare and lay a basis for future research at the neurological ICU.

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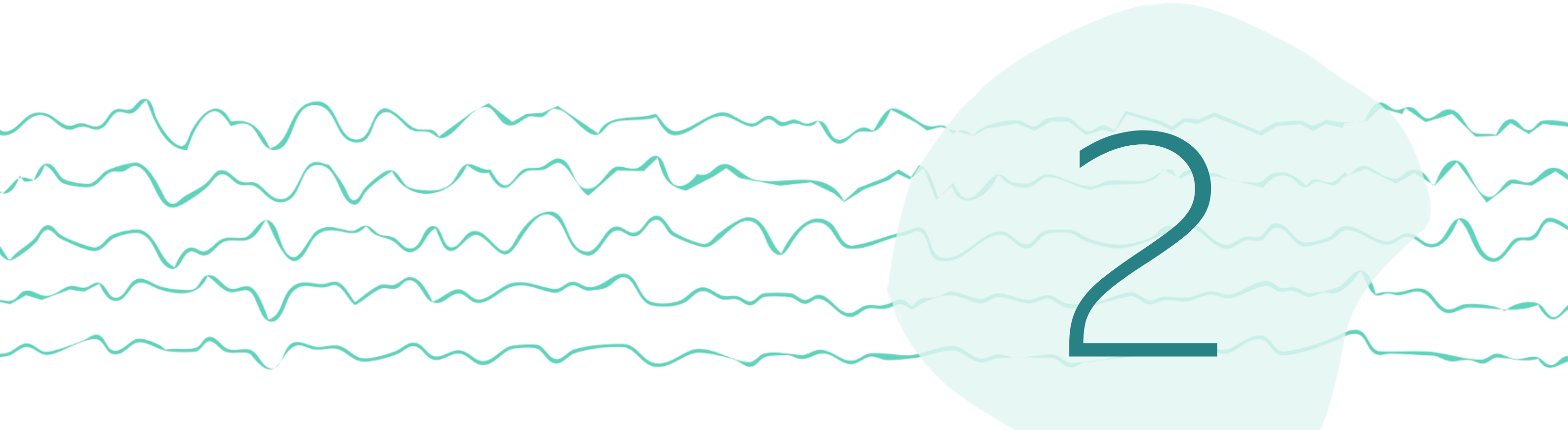


2

OPTIMISING NEUROMONITORING AT THE ICU

INVESTIGATING CURRENT WORKFLOW AND IDENTIFYING BARRIERS & FACILITATORS FOR CHANGE

Abstract

Background: The interest in continuous electroencephalography (cEEG) monitoring in critically ill patients is increasing, but practical challenges hinder widespread implementation. In this qualitative study, we evaluated the current EEG monitoring workflow at the ICU and aimed to identify potential barriers and facilitators for effective implementation of EEG monitoring at the Intensive Care Unit (ICU) of the Erasmus Medical Centre (EMC) in the Netherlands.

Methods: Semi-structured interviews were conducted with healthcare-, and research professionals from different departments, including EEG technicians, nurses, neurologists, and (neuro)scientists in both individual as well as focus group interviews. The Consolidated Framework for Implementation Research (CFIR) was used to guide the development of interview guides, coding manuals and a questionnaire.

Results: A total of 12 individuals, and two focus groups (n=4, and n=9) participated in the interviews conducted between January and March of 2023. The data were analysed using 23 of the CFIR constructs. Overall, the respondents described the current EEG monitoring workflow in positive terms. They described their willingness to adapt the workflow to be able to increase the effectiveness of EEG monitoring. However, the lack of interdepartmental communication, the high workload of EEG monitoring for many individuals involved, and the potential of overdiagnosis were identified as some of the most important barriers for the implementation of a new EEG monitoring workflow at the ICU.

Conclusion: This study identified several challenges for the implementation of a new EEG monitoring workflow at the ICU of the Erasmus MC. EEG monitoring at the ICU in general was perceived as having high potential in influencing clinical management and improving healthcare. However, several potential barriers were identified. The assessment of the current situation and the identification of perceived barriers and facilitators should be used for the development of an implementation plan.

2.1 Introduction

The interest in monitoring in critically ill patients is increasing, since it is currently the only clinically available diagnostic tool for the continuous monitoring of cerebral functioning. [1] Although the use of electroencephalography (EEG) in critically ill patients provides insightful information on the patients cerebral functioning, the practical use of EEG remains a challenge, which hinders widespread clinical implementation. [2] EEG recording in the Intensive Care Unit (ICU) is highly labour intensive, as a trained EEG technician should be available 24 hours a day to connect and maintain the EEG electrodes. Additionally, visual EEG interpretation should be performed by a trained clinical neurophysiologist at least twice a day, and is often performed every one to two hours. [1, 3] Furthermore, ICU patients are often repositioned and transported, which complicates the quality of electrode placement. Lastly, in patients with head trauma, placement of electrodes on the skin might not always be possible due to for example wounds or when part of the skull is removed. Due to these difficulties, EEG is not used in a broad variety of critically ill patients yet.

The current golden standard to assess the neurological status of these patients is the Glasgow Coma Scale (GCS), a tool to evaluate a patient's level of consciousness and neurological functioning based on their eye, motor, and verbal responses. [4] To reliably perform this assessment, sedatives need to be withheld. This potentially leads to an uncomfortable situation for the patients, and is not contributing to the patient care. Therefore, a non-invasive, real-time neuromonitoring tool like the EEG is desired. In 2018, Hilkman et al. performed a national survey on the use of cEEG in the ICU in the Netherlands. [5] They showed that cEEG is increasingly used in Dutch hospitals, however some barriers for a more widespread implementation were identified. The authors concluded that future research should focus on lowering cEEG workload and improving (quantitative) assessment, interpretation, and reporting to be able to increase research possibilities, and most importantly improve patient healthcare. The current study was performed in preparation of the implementation of new EEG equipment at the ICU of the Erasmus Medical Center Rotterdam (EMC), with the aim to decrease the current workload, increase research possibilities and improve patient healthcare.

2.1.1 Objectives

The main goal of this study was to identify pitfalls, wishes and opportunities for improvement in the current EEG neuromonitoring workflow at the ICU of the EMC. To obtain a better understanding of how to implement new EEG equipment at the ICU, a qualitative study among health care professionals of different departments, involved with EEG monitoring at the ICU, was performed. The aims of this qualitative study were:

1. To evaluate the current workflow regarding EEG monitoring at the ICU
2. To identify the wishes, opportunities and general view of EEG monitoring in critically ill patients
3. To identify potential barriers and facilitators for the implementation of new EEG equipment and/or change in the current workflow at the ICU

2.2 Methods

2.2.1 Study design and participants

A qualitative study among health care professionals from different departments of the EMC was conducted. Health care professionals that were interviewed included three staff-members of the Clinical Neurophysiology (CN) department, the Physician Assistant (PA) of the CN department, and a neuro-intensivist and two nurses (neural practitioners) of the ICU. Additionally, we conducted two focus group interviews. The first group consisted of EEG technicians of the CN department, and the second group consisted of CN residents (Arts (niet) In Opleiding tot Specialist (A(N)IOS)). Healthcare professionals with different functions were interviewed individually, to limit the influence of social desirability (where responders answer in a way they think will make them look good). [6] Additionally, we interviewed a neurologist with regular ICU shifts, a neuroscientist with a focus on research involving neuromonitoring techniques, and a pediatric neurologist responsible for the implementation of amplitude-integrated electroencephalography (aEEG) at the Pediatric Intensive Care Unit (PICU) of the EMC. Finally, we interviewed a scientist of the Delft Laboratory for NeuroMuscular Control (NMC Lab) on aims for future research, and requirements for EEG equipment for neuromonitoring at the ICU.

2.2.2 The Consolidated Framework for Implementation Research

The Consolidated Framework for Implementation Research (CFIR) was first published in 2009, [7] and updated in 2022. [8] In the CFIR, five implementation domains are defined: characteristics of innovation, outer setting, inner setting, characteristics of individuals involved, and the implementation process. These five domains contain a total of 39 constructs that are related to different aspects of implementation. These constructs can be used to identify potential barriers and facilitators for effective implementation and are often used in the healthcare setting. Damschroder et al. (2022) recommend that researchers may select the most relevant constructs for their specific study setting. [8] In this study, we considered 23 constructs relevant for the interviews (Table 2.2). These constructs were used to develop the interview guide and coding manual that was used for the analysis of the data.

2.2.3 Interview guide development

Interview guides were developed based on the three main objectives described in Section 2.1.1. We mainly used the CFIR to guide questions with the aim of identifying the potential barriers and facilitators for implementation. The interview guide was developed in the Dutch language and adapted based on the different groups of healthcare professionals that were interviewed to account for relevant discrepancies between roles and tasks of participants (Supplementary Material A). Furthermore, we performed a pilot interview with a clinical neurophysiologist (and supervisor of this project). The goal of this pilot interview was to be able to add, remove, or alter questions and their order, before starting interviews with respondents as described in Section 2.2.1. Interviews were first conducted with respondents that were not directly involved with the current EEG monitoring workflow at the ICU, before interviews with employees that were involved with the workflow took place. This way, the suggestions provided during the former interviews could be tested during the latter.

2.2.4 Data storage & privacy

Before each interview took place, we provided participants with general background information through an information letter, and they were given the opportunity to ask questions before written informed consent was obtained. Recordings were removed after transcription, and the transcriptions were anonymously stored. Data was available to the interviewer only, and supervisors were provided with the results as described in this chapter only. To comply with privacy laws, transcripts of the interviews were deleted at the time of the completion of the study.

2.2.5 Interview procedure

Data was gathered through semi-structured in-depth interviews. The interviews were conversational, meaning that the different topics were discussed in an order that could vary per interview, but we planned the key-questions. The interview guide consisted of three different parts. In the first part, the general concept and goals of the implementation project were introduced and participants were asked to describe their function, their part in the current EEG workflow (if applicable), and their experience with EEG at the ICU of the EMC. Secondly, the participants view on the opportunities of EEG monitoring were discussed. The final part consisted of questions relevant for the specific function of the interviewee. Instead of questioning participants directly about the CFIR constructs, we aimed the questions more at the five domains of the CFIR. This way, interviewees were able to emphasise topics that they considered important, and initial wording bias was reduced. [6]

All interviews were conducted in the Dutch language, and aimed to last for 30-45 minutes. We recorded the interviews using a voice recorder on an iPhone 11 and manually transcribed them afterwards. Quotes used in Section 2.3 were translated into English.

Table 2.2: The selected 23 constructs used in this study, spread out over the five domains as defined by Damschroder et al. (2022) in the Consolidated Framework for Implementation Research (CFIR). [8]

Innovation Characteristics	
Relative Advantage	The innovation is better than other available innovations or current practice
Triability	The innovation can be tested or piloted on a small scale and undone
Complexity	The innovation is complicated, which may be reflected by its scope and/or the nature and number of connections and steps
Outer Setting	
External Pressure	
Performance Measurement	Quality or benchmarking metrics or established service goals drive implementation and/or delivery of the innovation
Local Attitudes	Sociocultural values (e.g., shared responsibility in helping recipients) and beliefs (e.g., convictions about the worthiness or recipients) encourage the Outer Setting to support implemenation and/or delivery of the innovation
Inner Setting	
Access to Knowledge & Information	Guidance and/or training is accessible to implement and deliver the innovation
Available Resources	Resources are available to implement and deliver the innovation
Space	Physical space is available to implement and deliver the innovation
Mission Alignment	Implementing and delivering the innovation is in line with the overarching commitment, purpose, or goals in the Inner Setting
Relative Priority	Implementating and delivering the innovation is important compared to other initiatives
Compatibility	The innovation fits with workflows, systems, and processes
Tension for Change	The current situation is intolerable and needs to change
Culture	There are shared values, beliefs, and norms
Human-Equality	... about the inherent equal worth and value of all human beings
Recipient-Centeredness	... around caring, supporting, and addressing the needs and welfare of recipients
Deliverer-Centeredness	... around caring, supporting, and addressing the needs and welfare of deliverers
Learning-Centeredness	... around psychological safety, continual improvement, and using data to inform practice
Communications	There are high quality formal and informal information sharing practices within and across Inner Setting boundaries (e.g., structural, professional)
Structural Characteristics	Infrastructure components support functional performance of the Inner Setting
Physical Infrastructure	Layout and configuration of space and other tangible material features support functional performance of the Inner Setting
Information Technology Infrastructure	Technological systems for tele-communication, electronic documentation, and data storage, management, reporting, and analysis support functional performance of the Inner Setting
Work infrastructure	Organisation of tasks and responsibilities within and between individuals and teams, and general staffing levels, support functional performance of the Inner Setting
Individual Characteristics	
Motivation	The individual(s) is committed to fulfilling the Role
Capability	The individual(s) has interpersonal competence, knowledge and skills to fulfill Role
Need	The individual(s) has deficits related to survival, well-being, or personal fulfillment, which will be addressed by implementation and/or delivery of the innovation

2.2.6 Questionnaire

In addition to the semi-structured interviews, we developed a questionnaire for EEG technicians with questions of a quantitative nature. Participants were asked to rank multiple quotes on a scale from strongly disagree to strongly agree. Additionally, we asked them to rank several of their regular tasks in order of personal priority, and in order of the most to least time consuming tasks. The author was present during the time in which the EEG technicians participated in the questionnaire to be able to provide extra information on the questions when needed. Data was collected using Google Forms. The questionnaire can be found in Supplementary Material D.

2.2.7 Analysis

For the analysis of the data, two different coding manuals were developed using a thematic approach. [9] To address the first two aims of this study (Section 2.1.1), we developed a coding manual using an inductive approach. To address the third aim, a second coding manual was developed. For the second coding manual, we used a combination of a deductive and inductive approach. The basis of the coding manual was theory-driven, based on the 23 constructs of the CFIR framework as described in Table 2.2. The constructs of the CFIR framework were used at the aspect level. Based on the transcripts, we selected statements of one or few sentences as fragments and coded them using the open source qualitative data analysis application QualCoder. [10] For every new issue that was discussed, a new fragment was started. During this process, we used an inductive approach to create new codes for further refinement at the level of aspects. Additionally, codes that were used ≤ 1 times were reconsidered and pooled with other codes if applicable. All fragments that were coded, were additionally coded with a positive (+) or negative (-) association. Positive associations were interpreted as facilitators, whereas negative associations were interpreted as barriers. The complete coding manuals that we used for the data analysis in this study can be found in Supplementary Material B. To enhance trustworthiness, the results were analysed in a stepwise manner. [11] This started with the interview guide development in collaboration with the supervisor of this project. Additionally, two interviews were coded by a fellow student to be able to establish inter-rater reliability (automatically calculated in QualCoder using Cohen's kappa (κ) statistics) and therefore increase the objectivity of the analysis. [6]

2.3 Results

2.3.1 Interview characteristics

Two focus groups and 12 individual interviews were conducted between January and March 2023. The focus groups of the residents, and EEG technicians consisted of four and nine respondents respectively. Respondent characteristics can be found in Table 2.3. The mean duration of the individual interviews was 36 minutes and 52 seconds (range: 25m38s - 42m18s), and the two focus group interviews lasted for 32m31s and 32m45s. For the coding manuals on the current workflow and barriers and facilitators, a κ of 0.816 and 0.732 was achieved respectively.

2.3.2 EEG monitoring at the Intensive Care Adults of the Erasmus MC

Aspects of the current workflow of EEG monitoring at the ICU Adults were discussed in 13 out of 15 interviews. In the remaining two interviews (both scientists, respondent 3 & 4) we did not discuss this subject as the respondents were not directly involved in the monitoring workflow. The main categories that we discussed were the logistics of the current workflow, the (possible) indications for EEG monitoring at the ICU, and the technical requirements for optimal EEG monitoring. The results presented in this section are grouped based on these categories.

Logistics

Providing high-quality healthcare in the intensive care unit (ICU) starts with a collaborative effort between various healthcare professionals, including the ICU nurse, ICU resident, and intensivist. The ICU nurse is present in the patient's room for the majority of the time and is responsible for providing hands-on care to the patient, including the administration of medications, monitoring of vital signs, and ensuring that the patient is comfortable. The ICU resident, together with the ICU staff, is responsible for overseeing the patient's care plan and deciding on monitoring- and treatment. The full ICU team ensures that the patient's medical needs are being met and that care is delivered in a timely and effective manner.

In case of a neurological patient, the ICU team usually decides to consult the department of neurology. The neurology resident tends to be consulted by the ICU resident for the treatment of patients with neurological disorders such as a stroke, seizures, loss of consciousness, and brain infections. The neurology resident then physically visits the ICU patient to evaluate the patient's neurological status, and

Table 2.3: Respondent characteristics. ^{a}: Face-to-face interview. ^{b}: Microsoft Teams interview. *: pilot interview. BmE: Biomechanical Engineering. TUD: Delft University of Technology. AIOS: Arts In Opleiding tot Specialist. NP: neural practitioner.

N	Function	Department	Type
1^a	Neurologist - CN	Clinical Neurophysiology	Individual*
2^a	Neurologist (Pediatric)	Pediatric Intensive Care Unit	Individual
3^b	Scientist	BmE, 3mE, TUD	Individual
4^a	Scientist	Neuroscience	Individual
5^a	Physician Assistant	Clinical Neurophysiology	Individual
6^a	Neurologist - CN	Clinical Neurophysiology	Individual
7^b	Intensivist	Intensive Care Unit	Individual
8^a - a	Resident (AIOS)	Clinical Neurophysiology	Focusgroup
8^a - b	Resident (AIOS)	Clinical Neurophysiology	Focusgroup
8^a - c	Resident (AIOS)	Clinical Neurophysiology	Focusgroup
8^a - d	Resident (AIOS)	Clinical Neurophysiology	Focusgroup
9^a	Neurologist - CN	Clinical Neurophysiology	Individual
10^a	Neurologist - CN	Clinical Neurophysiology	Individual
11^a	Senior nurse - NP	Intensive Care Unit	Individual
12^a - a	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - b	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - c	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - d	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - e	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - f	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - g	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - h	EEG technician	Clinical Neuropohysiology	Focusgroup
12^a - i	EEG technician	Clinical Neuropohysiology	Focusgroup
13^a	Nurse - NP	Intensive Care Unit	Individual
14^a	Neurologist	Neurology	Individual

to advise about the adjustments of treatment plans as needed. Subsequently, the neurology resident and staff-members discuss the patient and can provide expertise in additional monitoring techniques like the EEG, which can provide valuable information about the functioning of the brain and the patient's prognosis.

Not all neurological patients in the ICU are monitored using EEG. In case of an indication for EEG monitoring, the CN resident is consulted by the neurology resident. Together with the CN staff, it is decided whether the ICU patient needs EEG monitoring. Subsequently, the EEG technician is asked to attach the EEG electrodes to the patient's scalp. Depending on the indication for EEG monitroing, this usually means either the attachment of 21 or 13 electrodes (Figure 2.5). Furthermore, the EEG technician is responsible for troubleshooting any technical issues that arise during the test and for ensuring that the equipment is properly maintained. After attaching the EEG electrodes, several tests can be performed depending on the indication for EEG monitoring. The CN resident and staff then assess the EEG at specified intervals and refer results back to the neurology resident, who after discussion with his/her supervisor refers back to the ICU team to provide them with advice regarding optimal treatment of the patient. Figure 2.4 provides an overview of the workflow described above.

Logistic wishes

Interviewees were asked to describe their thoughts on the possible improvement of the current workflow. A summary of all suggestions can be found in Supplementary Material E, Table E.3. Among other things, it was mentioned how shifting tasks within the CN department, implementing automatic assessment of the EEG, and defining responsible employees per involved department would lead to a better workflow.

> “You could think of appointing an employee, like a neural practitioner or a physician assistant, or no wait a technical physician to the task of daily checkups on the EEG attachment or detachment of electrodes etcetera, who shows his or her face at the ICU every day or so.” - respondent 8c

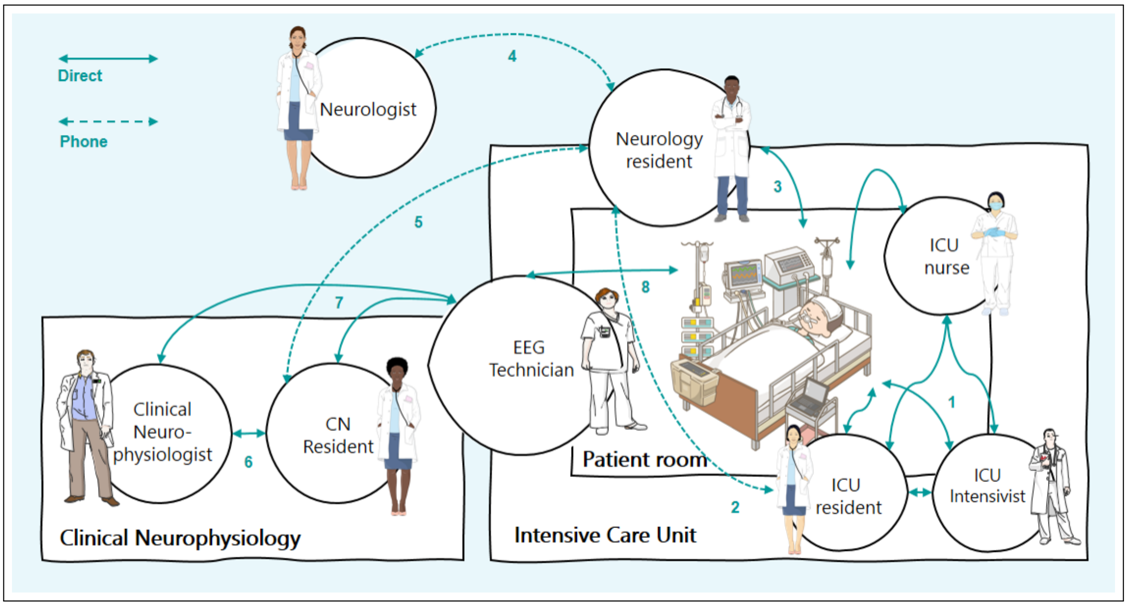


Figure 2.4: Overview of current workflow regarding electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) of the Erasmus Medical Center, Rotterdam. Three main departments are involved: the ICU, the department of neurology and the sector clinical neurophysiology (CN) as part of the department of neurology. Numbers 1-8 reflect the order of communication between different healthcare workers, starting with an ICU patient and ending with the EEG technician attaching the EEG electrodes. Physical locations of healthcare workers are represented by the circles surrounding them. The teal arrows represent the method of communication between all individuals involved. Parts of the figure were drawn by using pictures from Servier Medical Art. Servier Medical Art by Servier is licensed under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/).

Efficiency

When we asked respondents about the efficiency of the above described workflow, they mentioned that the constant discussion between different departments and within departments regularly causes significant delay in optimal treatment and/or feedback from one department to the other.

> “What we often notice is that the neurology resident has visited the patient, but then continues to visit several other patients before contacting his or her supervisor. And then at our section (CN) this happens again and eventually without noticing, it takes hours before the EEG gets attached.” - respondent 9

Although the current workflow is not experienced as efficient, respondents described the structure of an academic teaching hospital, where such a workflow is standard practice and neither residents nor staff members can or should be bypassed. In peripheral hospitals in the Netherlands, there often are less people involved in the entire workflow. However, implementing a similar workflow in the EMC would take away the learning opportunity of residents. When asked about the possibility of bypassing the neurologist for some of the indications, most respondents indicated that they see no advantage in this, since the current workflow ensures the efficient triage of indications.

> “This way, we have a good triage. If you remove the neurologist from this workflow, you take the risk that there will be a way too high demand on EEG monitoring without a good indication. At the ICU, they often find it hard to make the correct assessment. Not surprising, as they know a lot of other things.” - respondent 6

Indications

Respondents agreed on four indications when we discussed indications for EEG monitoring at the ICU, namely: monitoring in postanoxic encephalopathy, monitoring treatment effect of treatment in Non Convulsive Status Epilepticus (NCSE)/Status Epilepticus (SE), rule out NCSE, and monitoring a burst-suppression pattern in patients with elevated Intracranial Pressure (ICP) or NCSE, who are kept in a barbiturates coma (Table 2.4). In some cases, debates among clinical neurophysiologists, neurologists,

Table 2.4: Indications for electroencephalography (EEG) monitoring at the intensive care unit (ICU) of the Erasmus MC (n. of respondents = 12). The current monitoring indications are described under clinical practice. Research indications are described in the second half of the table. cEEG: continuous EEG. NCSE: non convulsive status epilepticus. LOC: loss of consciousness. CABG: Coronary Artery Bypass Grafting. VA-ECMO: VenoArterial ExtraCorpeal Membrane Oxygenation. ICH: Intracerebral Hemorrhage. SAH: Subarachnoid Hemorrhage. ICP: Intracranial Pressure. TBI: Traumatic Brain Injury.

Clinical Practice

	Indication	Protocol	Goals
01	Postanoxic coma	National guideline, cEEG 12h and 24h post cardiac arrest	Providing neurological prognosis
02	Refractory NCSE	cEEG	Monitoring treatment effect
03	Unexplained LOC	standard EEG	Rule out NCSE
04	Pentobarbital coma	cEEG	Monitoring sedation depth

Research

	Indication
01	Early ischemia detection High stroke risk: coagulation dissorder, embolism, risk on embolism after surgery, CABG, VA-ECMO Bleeding: ICH, SAH
02	Tracking changes in ICP in patients with TBI
03	Using the EEG for the neurological prognosis of ICU patients, especially in TBI
04	Monitoring more frequently without a direct question relevant to the clinic or research
05	All patients with a medical history of epilepsy, due to a higher risk of recurrent epileptic abnormalities
06	Early detection of delirium
07	Meningitis detection and prognosis
08	Prognosis in autoimmune encephalitis
09	Differentation in causes of metabolic encephalitis

and the ICU about the indication and added clinical value for EEG monitoring were described.

> "Every now and then there is some discussion about the indication. There are requests when the initial suspicion of epilepsy is relatively low quite regularly. And in most cases, there are no epileptiform discharges. However in the current practice, the EEG is attached anyway. This is to prove that there is no NCSE and immediately afterwards the EEG can be detached. At least, that is what you hope for." - respondent 8b

It was highlighted how it is important for all specialists to work together to determine the appropriate indications for EEG monitoring in the ICU, and to keep discussing those indications over the coming years. This involves careful evaluation of the patient's medical history, clinical symptoms, and other diagnostic tests, as well as consideration of the potential clinical consequences of EEG monitoring.

A large variety of indications was mentioned when we asked respondents about the potential added value of EEG monitoring in the critically ill. These indications are summarised in Table 2.4. The indications that were mentioned can be roughly divided in monitoring to detect neurological complications early on, to diagnose patients, and to provide a prognosis. Furthermore, some respondents explained their interest in the monitoring of the brain as a vital organ, without feeling the need to have a clear question and/or proven added value.

> "Sometimes I think you do not need the added value, but it should be enough that you can just monitor the brain. For your understanding of the patients condition, what is really happening?" - respondent 11

Research wishes & requirements

Interviewees explained different interests and goals when it comes to exploring EEG monitoring possibilities at the ICU. A common theme was that research on the use of EEG at the ICU should focus on the impact on clinical decision making and patient outcome. Clinicians were primarily interested in using EEG monitoring to improve patient outcomes, support treatment decisions, and monitor alteration of EEG patterns over time,

> "Because you have a problem of the brain. And you wish to monitor how this problem evolves. What are the changes over time, if any? The specific question would be: what can the EEG add to that? Actually, we do not

> know that, but that would be the added value of EEG monitoring in my opinion." - respondent 7

while scientists for example were more interested in exploring new EEG monitoring techniques, such as high-density EEG, that can potentially provide more detailed information about brain function and help diagnose neurological conditions more accurately. When we asked questions about research possibilities, respondents described their interest in using EEG monitoring to gain a better understanding of the brain's response to critical illness or injury, and to identify new biomarkers or treatment targets. Additionally, interest in developing new analytical tools or algorithms that can process large amounts of EEG data and extract meaningful insights were described, mainly in order to reduce the workload that currently comes with assessing EEG recordings and at the same time increase the monitoring effectiveness.

> "I can imagine that the current digitalisation and Artificial Intelligence (AI) could reduce the labour intensiveness of EEG assessment. If this is doable anywhere in neurology, I believe it is within the CN department." - respondent 14

> "Algorithms of EEG signals would make EEG monitoring applicable and understandable for non-expert users. I believe that Machine Learning and other AI would be especially suitable for implementation of the EEG. Not only to be used by everyone who likes, but especially for the ICU nurses who are at the patients bedside 24 hours a day. And in addition to that, it could help with questions like: what does this signal mean and when do we need to intervene?" - respondent 7

However, not all respondents had full trust in the possibilities of AI. It was often mentioned how AI could be helpful in reducing the workload of visual assessment of the EEG, but how current algorithms have failed to accurately handle the several artefacts that the EEG is prone to. A summary of all discussed research possibilities can be found in Supplementary Materials E, Table E.5.

Technical requirements

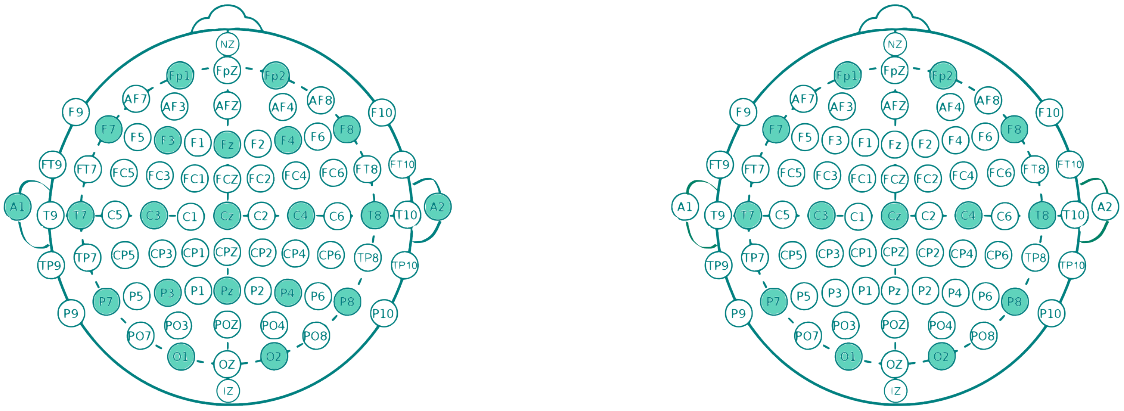
The majority of respondents mentioned they could not give input on the technical requirements for EEG equipment. However, the input that was received is summarised in Supplementary Materials E, Table E.4. Mainly, thoughts on the amount of necessary electrodes were shared. For three out of four indications in clinical practice, an EEG montage with 21 electrodes is used (Figure 2.5a). When the national protocol for the EEG monitoring of postanoxic patients came into effect in 2019, this montage was used as well. However, by the end of 2021, through trial and error it was found that using a reduced montage was sufficient for determining the EEG background pattern. To reduce the labour intensiveness, it therefore was decided to only attach the 13 electrodes as shown in Figure 2.5b. Respondents shared the belief that the amount of electrodes required depends on the indication for EEG monitoring. The general opinion was that in case of epilepsy, localisation of the measured electrical potentials is important and therefore at least 21 electrodes are needed.

> "But we should not get too worked up about that, it is not like we know the exact location right now. Maybe we even need more electrodes, and exact localisation is not even possible using EEG anyways." - respondent 6

However, in case of diffuse diseases like ischemia after Out of Hospital Cardiac Arrest (OHCA) or to detect asymmetry, respondents believed a reduced montage would suffice. In case of research on the other hand, it was noted that high-density EEG could pave the way for new opportunities in the calculation of EEG features such as functional connectivity.

> "All of our research is performed with at least 64 electrodes. Actually, 128 most of the time. However, that is time consuming. I think that we need at least 32 electrodes to calculate measures like the functional connectivity, but it would be better to have at least 64." - respondent 3

In the current workflow, EEG technicians manually attach each electrode one by one. We discussed several other EEG monitoring techniques, including the use of EEG caps (with all electrodes already attached according tot the 10-20 or 10-10 system) instead of single electrodes or using less electrodes if possible. Views on the usage of caps varied: in general, it was mentioned how caps could not be used in case of epilepsy, because little movement of the caps and thus electrodes would disturb localisation.



(a) Regular 10-20 montage with 21 electrodes

(b) Montage with 13 electrodes, used for prognosis in postanoxic encephalopathy

Figure 2.5: Electroencephalography (EEG) electrode locations and montages used for different indications at the Intensive Care Unit Adults of the Erasmus Medical Center.

However, for usage with different indications and in particular for research purposes, respondents saw more benefit in using EEG caps. Not only was it mentioned how caps would allow for high-density EEG recordings, respondents also thought caps would potentially allow for attachment by ICU nurses instead of EEG technicians for some indications. Concerns about using caps were mainly regarding signal quality, especially the reduction of quality over time.

> “I do think we could use caps. However, in case of continuous long-term monitoring, we know that the signal quality reduces.” - respondent 9

The opinions of EEG technicians on the usage of EEG caps were divided. Technicians with experience using caps were mainly positive, while technicians without experience mentioned all disadvantages and were doubtful about the time that would be gained using the caps instead of individual electrodes.

> “Yes but the hair. We recently had someone who had been lying in the mud for 12 hours, that would not work using a cap. And more often we have people with head trauma and drains. At this moment that does not even work. And I think I would prefer, I would be just as fast attaching single electrodes as using a cap.” - respondent 12f

2.3.3 Barriers & Facilitators

In total, 59 barriers and 49 facilitators for the implementation of a new EEG monitoring workflow were identified (Supplementary Material F). The barriers and facilitators that captured the common thread are summarised per domain of the CFIR below.

Innovation characteristics

Respondents noted that EEG monitoring could significantly influence clinical decision making. However, the majority had trouble with the fact that for most indications, no strong evidence is available yet. Although EEG monitoring at the ICU was perceived as a useful tool to monitor the patients brain function in a non-invasive matter, the relative advantage was questioned as well.

> “I think there is an enormous effect of confounders that you cannot always correct for. I believe part of the prognostic value of EEG lies within factors that can be observed from the outside as well. So the fact that you can identify biomarkers is not the same as ‘The EEG has prognostic value’.” - respondent 14

When asked about the complexity of EEG monitoring, respondents mostly saw this as a barrier. Examples of high complexity as a barrier were the complicated placement of EEG electrodes, as well as the interpretation of EEG recordings that requires trained experts. Furthermore, it was described how the EEG is prone to several artefacts like movement, sweat and other signals at the ICU. Respondents were concerned about how to interpret the EEG when it would be used for new indications.

> "To what kind of EEG abnormality would lead those [other indications]? Especially with less electrodes it is important to have that clear, otherwise this will lead to a lot of noise and overdiagnosis." - respondent 8a

However, the complexity of EEG measurements was noted as a facilitator as well.

> "Therefore [the complex nature of the EEG] I think this could potentially lead to a significant increase in knowledge." - respondent 5

Outer setting

Barriers in the outer setting were barely described, and facilitators were not described at all by interviewees. Barriers that were mentioned regarded the general resistance against change within a hospital, and the fact that the costs of healthcare in general cannot increase further. Additionally, attitudes towards implementing AI on neurophysiological signals in the acute setting might vary.

> "There is a lot of collaboration between the department of neurology and radiology in the acute setting. I cannot imagine the department of clinical neurophysiology being involved in the acute setting, that won't happen." - respondent 14

Inner Setting

In the current work infrastructure in the inner setting (i.e. all involved departments) some barriers as well as facilitators were identified. One of the barriers regarding equipment availability that was noted by respondents was that the hardware of the EEG monitors is not always available, even within the current practice. There are currently 5 monitors available, that are shared with the PICU, and these are also used during regular planned EEG recordings outside of the ICU.

> "So when every monitor is being used, that sometimes might be a problem. In the morning, right at the start of our shift, we have to kind of conjure up the equipment. No, but it can be a logistic nightmare." - respondent 10

Some facilitators mentioned were the configuration of ICU patient rooms that are designed with a considerable amount of space for monitoring equipment, the possibility of detaching electrodes from hardware in some indications to pause the recording and continue when the hardware is available again, and the tension for change regarding the possibilities of monitoring the brain at the ICU.

Respondents discussed that there is room for emergency EEG monitoring within the planning of EEG technicians, and that the planning can be easily adapted. Furthermore, the current infrastructure allows for precise triaging of patients. However, the current workflow is not always efficient and there is a shortage of EEG technicians.

> "There are not enough EEG technicians. When the technician gets called during their shift and has to come to the hospital during the night, they will not be here the following day and then the schedule of the next day sometimes has to be cancelled, because there are no technicians that can cover."- respondent 8c

Another important potential barriers could be a new law, stipulating recovery time after an on-call shift if residents are contacted at least twice during the night.

> "One bottle-neck would be that we will not be able to work during the day after a night shift. The law is to protect us, but it actually bothers the workflow. That way, we will not be able to increase the EEG monitoring." - respondent 8d

When we discussed the collaboration between the different departments involved, interviewees noted that they barely knew anyone outside of their own department. Explanations that were suggested were the size of the departments (e.g. 40 neurologists), and the size of the hospital in general.

> "I know only one person at the ICU, they are too far away. The hospital is too big for efficient collaboration. If you want this project to succeed, you have to arrange a meeting with all people involved. That would be a lot." - respondent 9

However, communication within departments was experienced as efficient and pleasant. CN staff, CN residents and EEG technicians all work on the same corridor, supporting accessibility of all employees. Interviewees discussed how at the CN department, everyone is open to discuss about almost everything and how there are clear rules and procedures. Furthermore, communication between the department of neurology and CN were mentioned as being pleasant. Even though specialists do not always agree, communication supports the decision making process.

> "Almost all the time it is not a yes or a no, it is about the indication and how quick do we need the EEG? We almost always talk it through and find a solution, come to a middle ground." - respondent 10

When inquired about the possibility of increasing the number of patients monitored at the ICU, the CN staff and residents considered the current workflow and concluded that some additional EEG monitoring could be accommodated within limits. The indication (and thus amount of time spent on reviewing the EEG) and the timing of visual assessment were noted as important factors when deciding whether extra monitoring would be possible.

> "That really depends on the amount of monitoring. In the current workflow where everyone reviews the entire EEG, I don't think this would be a good idea. However, one extra EEG monitoring per week would not be a problem, if we don't have to review during the night. It all depends on what we impose on ourselves." - respondent 6

Interviewees mentioned how the use of AI would significantly increase the possibilities of both the amount of EEG monitoring that would be possible as well as the yield that would be achieved by EEG monitoring.

Furthermore, an aspect that the entire CN staff, CN residents, and neurologists referred to and kept bringing up was the availability and experienced workload of EEG technicians.

> "I think the biggest and actually only real problem would be the EEG technicians, they will not be able to increase their work."- respondent 8a

However, when we asked the EEG technicians themselves about the experienced workload, they mentioned that due to the involvement of the CN staff, the workload they experienced was not that high and that they did in fact see ways to create room for an increased demand on their activities.

> "The staff actually really makes their way to ensure that our tasks remain doable, I really appreciate that. I do think there is room for increased EEG monitoring within our planning, but until a certain amount. We would just have to try and evaluate."- respondent 12g

Although both ICU nurses did not think the workload on a regular day at the ICU was that high, they mentioned the high workload of the "wake-up call" they perform daily in patients with a (potential) high ICP. During the wake-up call, sedatives are withheld for approximately 30 minutes and the patients has to be neurologically scored after these 30 minutes.

> "Some patients can get really wild, and then it has a really high workload for us, since it is our task to contain the patient. Some patients react with a sky-high blood pressure and then you have to get that under control before you can continue on. Yes, but some patients do not respond." - respondent 13

Individual characteristics

First, the motivation to change and/or add to the tasks of the interviewees was discussed. All interviewees from the ICU were enthusiastic and motivated to change the current workflow. Especially the neural practitioners were willing to invest time into training colleagues in using EEG equipment, with the biggest driving force being their curiosity. Additionally, it was mentioned how many ICU nurses have affinity with neurological patients, and that motivation would be high among most of them, influencing the enthusiasm of the other ICU nurses.

> “I think that if there are some superusers with a lot of knowledge and motivation, and we teach the remaining nurses at the bed-side and provide regular training and mention the potential added value, people are willing to learn.” - respondent 11

Furthermore, all respondents were curious to see what a more extensive EEG monitoring workflow would add in terms of new insights and possible influence on treatment plans, which was described as a key factor in the motivation of the interviewees. Although motivation amongst interviewees was high, some potential barriers were described as well.

> “Left or right, this means extra work. You need the commitment of all involved people, and as long as the added value has not been proven yet, they may lack motivation.” - respondent 10

When discussing the capabilities of the individuals involved, opinions varied. Some facilitators that were mentioned were that the EEG technicians are well trained, in general there is a lot of shared knowledge at the CN department, and the employees of the ICU are familiar with change and technical equipment and implementations. However, it was often mentioned how, based on experience at the PICU, ICU nurses often do not know how to attach EEG electrodes the right way, even after training.

> “With aEEG at the PICU we have seen that the electrodes aren’t attached the right way at all times. Even though there are protocols available to them [the ICU nurses].” - respondent 5

Furthermore, the EEG signals are often misinterpreted at the ICU, due to the high complexity of the signals.

> “Intensivists know a little about a lot, that’s how I see it. And sometimes they cross their own borders. They think they see something relevant, but they actually do not know how to interpret the EEG. Some do, but most of them do not.” - respondent 8a

2.3.4 Questionnaire

A total of 9 out of 12 EEG technicians participated in the questionnaire right after the focus group interview was performed. Contrary to the viewpoint of a significant portion of the other respondents, EEG technicians expressed disagreement with the statement that work pressure was too high and stated that there was room for additional EEG monitoring within the current workflow. Furthermore, EEG technicians tend to spend more time than preferred on waiting, and less time than what would be preferred on participating in discussions. Results from the quote agreement tested in the questionnaire are visualised in Figure 2.6. Distribution of these votes can be found in Figure D.1 of the Supplementary Material D. Additionally, the ratio between time spent and priorities of specific tasks of EEG technicians can be found in Figure D.2 of Supplementary Material D.

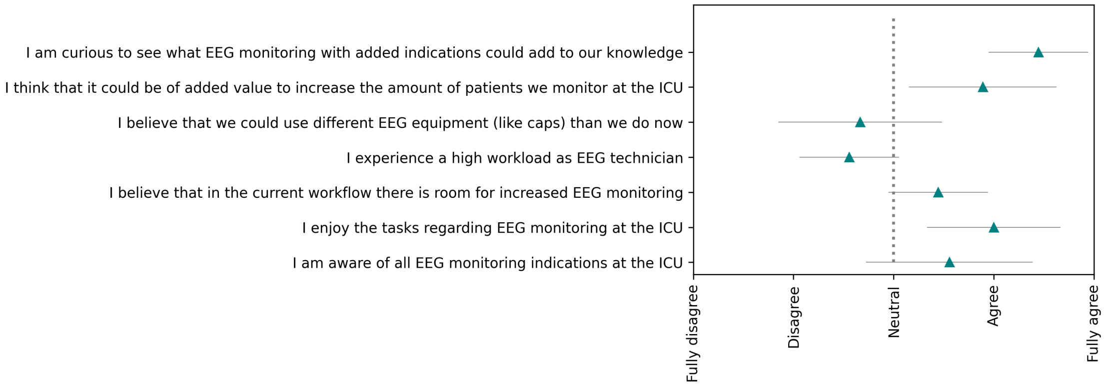


Figure 2.6: Electroencephalography (EEG) technician quote agreement (n=9). Teal triangles represent the mean vote, horizontal lines represent the standard deviation of the mean. ICU: Intensive Care Unit.

2.4 Discussion

In this study, we assessed the perspectives of several healthcare workers of the departments of neurology, clinical neurophysiology and the ICU of the Erasmus MC on EEG monitoring in critically ill patients. Additionally, views on clinical EEG research at the ICU were discussed. The interviews revealed several suggestions regarding the improvement of the current workflow and research, accompanied by factors that may facilitate or hinder the implementation of a new EEG monitoring workflow at the ICU.

2.4.1 Workflow and indications

The first two objectives of this study were to outline the current EEG monitoring workflow and to identify the wishes, opportunities, and general perspective regarding EEG monitoring in critically ill patients.

Current workflow and possible improvements

Overall, the EEG monitoring process in the ICU was positively experienced by the respondents. They concurred on the key indications for EEG monitoring and acknowledged their knowledge of when and whom to approach for assistance, which is considered one of the key factors for effective EEG monitoring as described by Alkhachroum et al. (2022). [2] The primary aspect for improvement in the current workflow that was identified was the interdepartmental communication. As research suggests that collaborative practice among interprofessional healthcare teams can result in improved patient outcomes and healthcare systems, all involved departments should strive to improve interprofessional collaboration. [12] Interviewees expressed a keen interest in improving and extending EEG monitoring to other indications in critically ill patients, particularly in the ICU, where there is a desire to monitor neurological patients without daily wake-up calls. Almost all respondents agreed that the primary objective of efforts to improve EEG monitoring should be to enhance brain monitoring efficacy in critically ill patients. To accommodate this interest, it is necessary to adjust the existing workflow to integrate monitoring for new indications, ultimately enhancing healthcare while considering everyone's preferences.

EEG monitoring at the ICU of the Erasmus MC

Currently, there are four indications for EEG monitoring at the ICU: monitoring in postanoxic encephalopathy, monitoring treatment effect NCSE/SE, rule out NCSE, and monitoring a burst suppression pattern in patients with a barbiturates coma. The indication with the most patients a year is the prognostication in postanoxic encephalopathy. A national protocol on this prognostication was implemented in the Netherlands in 2019. [13] The Erasmus MC ICU has monitored around 500 patients using EEG since the protocol's inception, making it the primary contributor. However, the impact on clinical decision-making remains unstudied, and some interviewees are skeptical about the added value of monitoring all these patients. Evaluating the added value of monitoring all postanoxic encephalopathy patients and identifying specific subgroups that may or may not benefit from such monitoring is therefore recommended.

A second large contributor is the monitoring of NCSE and Non Convulsive Seizures (NCSz). It is strongly recommended to use EEG monitoring to monitor NCSE and to detect NCSz in patients with primary brain injury like Traumatic Brain Injury (TBI), Subarachnoid Hemorrhage (SAH), Intracerebral Hemorrhage (ICH), and encephalitis. [1, 14] However, for patients without primary brain injury and unexplained lowered consciousness, there is a low level of evidence on the use of EEG to detect NCSE. [14] Despite the European Society of Intensive Care Medicine (ESICM)'s recommendations to use EEG monitoring to detect seizures in various diseases, the efficacy of such monitoring has not consistently yielded positive results on patient outcomes. [15–18] Lastly, according to a systematic review in 2017, there is currently insufficient evidence to determine the effectiveness of burst suppression therapy. While some literature suggests that it may be beneficial in reducing ICP and treating SE in specific cases, the circumstances under which it would be helpful remain unclear. Additionally, the impact of this therapy on a patient's functional outcome is not well established. [19]

Additional indications for EEG monitoring at the ICU

In addition to the current indications of EEG monitoring at the ICU, respondents suggested several additional indications. One of the frequently mentioned indications for EEG monitoring that could be further explored was the detection of brain ischemia in several diseases and/or treatments (SAH, ICH, stroke, and Veno-Arterial ExtraCorporeal Membrane Oxygenation (VA-ECMO)). The ESICM recommends using EEG to detect Delayed Cerebral Ischemia (DCI) in SAH patients, but the evidence on detecting ischemia in other diseases is lacking. [14] Ischemia caused by vasospasm after SAH can be treated if detected immediately. [20] Therefore, several attempts have been made to detect DCI in SAH early on, with promising results. [21] Furthermore, VA-ECMO increases the risk on neurological complications to up to 15% of the cases, and these complications are independently associated with a poor outcome. [22] Although treatment of these neurological complications could potentially lead to improved outcome, detection of these complications is often delayed. EEG has shown potential in identifying adult patients undergoing VA-ECMO who are at high risk of poor outcomes. Specifically, a suppressed background on the EEG and a lack of EEG reactivity have been found to be independently associated with unfavourable neurological outcomes. [23, 24] However, EEG studies in VA-ECMO patients are limited and caution should be taken when interpreting EEG recordings in these patients. [25] Another frequently mentioned aim of EEG monitoring was the non-invasive monitoring of ICP levels. Although only few case studies have explored this idea, some potentially helpful EEG features for monitoring elevated ICP have been identified. [26–28] Furthermore, non-invasive automatic prediction of ICP levels might be possible in the future, as was shown in a porcine model. [29] However, it is crucial to pay great caution when interpreting EEG recordings of patients who may be at risk of brain herniation. More research is necessary to fully understand any distinct EEG markers for these patients. [30]

2.4.2 Barriers & Facilitators

The third aim of this study was to identify barriers and facilitators for change in the current EEG monitoring workflow at the ICU. Barriers and facilitators were identified using 4 domains of the CFIR framework, of which 3 were extensively discussed: innovation characteristics, inner setting, and individual characteristics.

Innovation Characteristics

Although interviewees were positive about the exploration and implementation of EEG monitoring at the ICU and the EEG was acknowledged as the desired non-invasive neuromonitoring tool, we identified barriers as well. An important perceived barrier was that due to the complexity of the EEG, it requires specialised technical expertise to set up, calibrate, and interpret the results. This identified barrier has been widely acknowledged, [5, 31, 32] and therefore several EEG systems have been developed in order to reduce the complexity of application. [33–35] Furthermore, there is an increasing effort in the development of algorithms for the automatic assessment of EEG signals. [30]

Inner Setting

The inner setting refers to the internal context wherein the EEG is implemented, including the organisational culture, leadership, and available resources. [8] In this study, we defined the inner setting as the ICU and the CN department. Several factors that aid the inner setting include the abundance of knowledge and expertise within the concerned departments, the presence of multiple neurology-specialised healthcare professionals (both ICU nurses and intensivists), and the ICU's familiarity with technical implementation. To ensure efficient implementation and workflow, it is crucial to leverage these facilitating factors. Nonetheless, to achieve effective implementation, considerable attention must be paid to the workload of all healthcare workers involved. A significant point of disagreement which stood out was related to the workload of EEG technicians. Clinical neurophysiology staff and residents unanimously noted that the workload of EEG technicians would be a major impediment to increasing the amount of EEG monitoring. However, in the questionnaire, all EEG technicians reported being neutral or not experiencing a heavy workload and agreed that within the current workflow, EEG monitoring could be expanded. One possible explanation for this is that EEG technicians reported that the clinical staff takes measures to prevent an increase in their workload. Additionally, it is plausible that those EEG technicians who do experience a heavy workload did not show up to the focus group or may have resigned from their positions over the last few years. Nevertheless, the scarcity of available EEG technicians in the Netherlands remains a challenge, [36] and reducing the workload of EEG technicians should be a key priority in order to create space for additional and/or other tasks and ensure that EEG technicians do not become overwhelmed with work. Therefore, it is recommended to regularly assess and consider the preferences of EEG technicians. In addition to EEG technicians' workload, it is essential not to overlook clinical neurophysiologists and residents. While a few additional cases of EEG monitoring each month were deemed manageable, an extensive rise in EEG assessment could overwhelm their workload. Concerning the workload of ICU nurses, they stated that they would be willing to make some concessions, such as attaching EEG caps, if that meant that their workload could be alleviated in the future by potentially reducing wake-up calls, which should be further explored.

Individual Characteristics

The characteristics of the individuals involved in the implementation process, such as their knowledge, beliefs, and attitudes, can influence their acceptance and use of the intervention. [8] There was a significant variation in attitudes towards changing the current workflow, with varying reasons related to the barriers and facilitators mentioned earlier. Since the motivation of the individuals involved is crucial for successful implementation, recurring feedback sessions, clinical lessons, evaluations, etc. must be prioritised. Given the abundance of individuals involved who possess the suitable capabilities (like the physician assistant, neural practitioners and technical physician), their expertise should be utilised to organise these sessions and teachings to enhance and maintain the motivation of all participants.

2.4.3 Study strengths & limitations

One strength of this study lies in its recruitment of a diverse range of respondents, enabling the exploration of multiple perspectives. As a result, we achieved saturation of results for the first two objectives, indicating that additional data would not lead to any new themes. [37] To limit the influence of the extensive nature of the CFIR,[38] we excluded a selection of constructs that were deemed less relevant at the start of the study. However, some identified barriers and facilitators still warrant further investigation as saturation may not have been reached, and we advise to incorporate recurring evaluation meetings during the implementation phase to pinpoint any newly emerging barriers and facilitators. Furthermore, it is possible that a few barriers and facilitators were overlooked due to the absence of a definite implementation plan at the start of this study, a factor that was cited by some respondents as hindering appropriate feedback. Additionally, despite recruiting a diverse range of healthcare workers, some critical roles were excluded. Firstly, we recommended to involve the neurosurgery department, as they are usually consulted in TBI patients instead of the neurology department. Moreover, since the Erasmus MC ICU has two distinct sections, and all interviewees were from a single section (the general & trauma ICU), it is recommended to involve participants from the other section as well (cardio-thoracic ICU).

Another strength of this study was that during the data analysis, we incorporated additional codes into the coding manual using inductive analysis. However, the coding manual was not revised after coding all interviews, leading to some codes appearing only once. This happened particularly in the coding manual for the identification of barriers and facilitators. Nonetheless, we found that these codes did not overlap with different domains of the CFIR, and therefore the overall conclusions would not have been altered. Additionally, we believe that the merging of codes would not have impacted the identification of barriers and facilitators in the final analysis.

A final limitation of this study is that we did not discuss the cost-effectiveness of EEG monitoring at the ICU with any of the interviewees. Although a few participants did touch upon the significance of cost-effectiveness, the interview guideline was not tailored to elicit in-depth insights into this domain. As the cost-effectiveness has not been proven yet, further research on this topic is needed and should be a priority when elaborating an implementation plan. [39–41]

2.4.4 Future directions & recommendations

EEG equipment requirements

While certain critical factors concerning the necessary specifications of new EEG equipment have been established, a comprehensive overview remains elusive due to the limited input on this topic received thus far. It is therefore recommended to involve employees with exact knowledge on the monitoring equipment used in clinical practice, like the clinical physicist of the CN department. Once the most crucial requirements have been identified, all scenarios involving EEG measurements in the ICU setting ought to be documented. This approach will facilitate the evaluation of demo-models of new equipment in collaboration with vendors, enabling the selection of the most appropriate equipment for the given scenarios.

Furthermore, more research is necessary regarding the optimal number of electrodes to be used. While there is a desire in clinical settings to reduce the number of electrodes to decrease workload of EEG technicians and/or ICU nurses, the impact of this reduction on EEG assessment has yet to be investigated. On the other hand, from a research perspective, increasing the number of electrodes would be preferable. Ideally, a system capable of adjusting the number of electrodes as necessary would be implemented.

A final aspect regarding EEG equipment is the usage of AI and the development of algorithms to be able to automatically monitor the brain function. Using quantitative electroencephalography (qEEG), the numerical analysis of raw EEG signals, could reduce some of the workload of clinical neurophysiologists and thereby acknowledging an important barrier identified in this study. This area of both research and clinical application has experienced rapid advancement over the recent years. Hwang et al. (2022) concluded that with the ongoing advancement of qEEG techniques, which now incorporate machine learning, the utilisation of algorithms optimised for ICU settings holds the potential to significantly enhance quantitative scoring, and detect EEG patterns of interest with greater accuracy. [30] Utilisation of qEEG would also allow for future development of a dashboard with neurological parameters of the critically ill patients, a wish emphasised by all interviewees from the ICU.

Implementation process

The fifth domain of the CFIR, the implementation process itself, was not explored in this study, because of the early stage of orientation. The implementation process itself, including planning, engaging stakeholders, monitoring progress, and adapting to changing circumstances, is critical to the success of the intervention. [8] The most important factors that should be further explored for an effective implementation that we identified in this qualitative study were:

- Focusing on reducing the current workload first, to be able to increase the effectiveness of future EEG monitoring
    - It is important to closely consider the preferences of various healthcare professionals, as this study has revealed discrepancies in the perspectives of different interviewees
    - Regular assessment and feedback sessions should be implemented to encourage all individuals involved and to address any challenges that arise

- Improving the interdepartmental collaboration
  - Assigning a key-figure that stays in contact with all involved employees and has the final responsibility for the implementation process and regular evaluations
  - Assigning a responsible persons per department involved to create an implementation team
- Deciding on the most promising indications for EEG monitoring
  - Emphasis should be laid on the effectiveness of EEG monitoring, i.e. the influence on clinical management and patient outcome
  - Do not only consider new indications, but pay attention to the effectiveness of EEG monitoring in the current indications
- Exploring how to deal with the different ICU sections (general versus cardio-thoracic)
- Deciding on who and how to train for the application of new EEG equipment

Based on these identified factors, we considered different scenarios for the first phase of implementation. These scenarios, including pros and cons, are summarised in Supplementary Materials G. They can be combined to develop an implementation plan. However, after defining the first steps, there is still a need to develop a step by step guide on how to carry out each phase of the implementation.

Taking advantage of the diverse set of facilitators presented in this study, and considering the potential challenges, we believe that a successful implementation can be accomplished. As the goal of this study was to identify all relevant factors for an effective implementation, no definitive recommendations on the implementation itself can be provided yet. In 2022, Mosch et al. developed a framework for the implementation of health technology in the ICU setting and defined strategies for the pre-implementation phase including: identifying local needs, barriers and facilitators, selecting motivated staff from all involved departments, testing of usability, visiting other sites, and organising team meetings,[42] of which the latter four should be further elaborated upon. The subsequent phase involves devising an implementation plan, but prior to commencing this process, the considered (and possible additional) scenarios must be deliberated with personnel from all departments involved. The key to ensuring a successful implementation of EEG monitoring at the ICU of the Erasmus MC lies within fostering a interdepartmental team effort.

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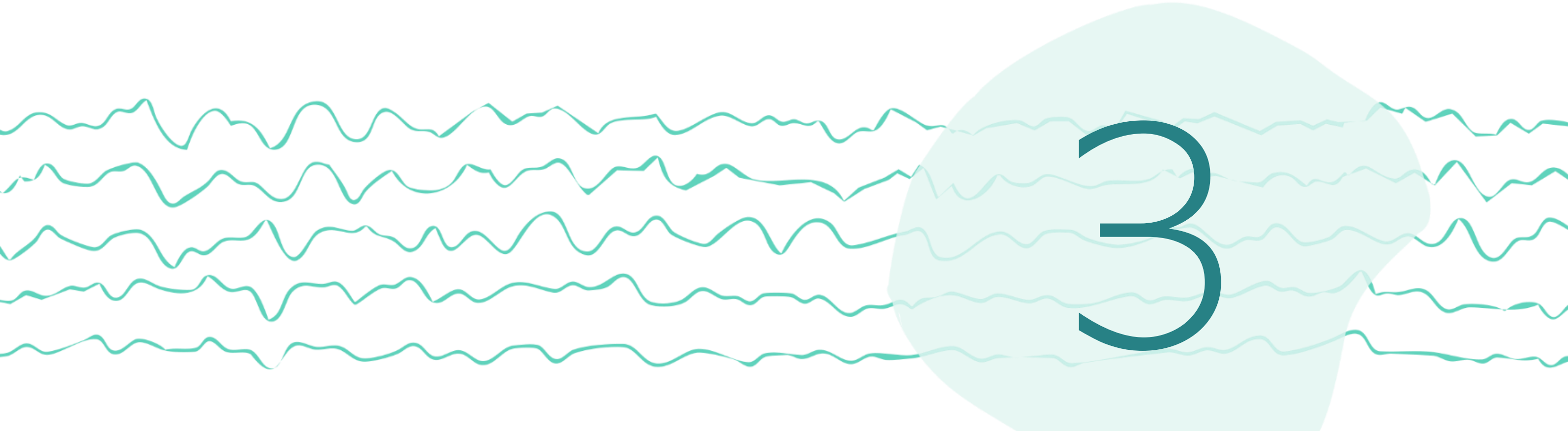


3

OPTIMISING NEUROMONITORING AT THE ICU

CLASSIFICATION OF BACKGROUND PATTERNS IN POSTANOXIC ENCEPHALOPATHY USING A REDUCED NUMBER OF ELECTRODES

Abstract

Background: Since 2019, a national guideline on prognostication after postanoxic encephalopathy is in place, describing several electroencephalography (EEG) background patterns associated with a poor or good neurological outcome. To reduce the labour-intensiveness and subjectiveness of visual EEG interpretation, in this study we developed a Machine Learning (ML) model for the automatic EEG background pattern classification in postanoxic encephalopathy. Additionally the effect of reducing the number of EEG channels used on model performance was evaluated.

Methods: EEG recordings with nine different background patterns of 327 patients with postanoxic encephalopathy were included in this study. For the automatic classification of EEG background pattern, a Random Forest (RF) classifier was developed based on a total of 26 quantitative electroencephalography (qEEG) features - averaged per epoch - per one of twelve EEG channels, initially. This was gradually reduced to 10, 8, 6, and 4 EEG channels. A stratified 5-fold cross-validation approach was employed to maintain the distribution of the different classes in both the training and test sets. Model performance was evaluated using a One-vs-Rest (OvR) approach to compute the Area Under the Curve - Receiver Operating Characteristics (AUC-ROC) for the primary outcome measure and the F1-score as the secondary outcome measure.

Results: RF classifiers were trained on eight background pattern categories. The micro-averaged AUC of the baseline model with a montage of 12 channels was 0.923 (95% CI: 0.918-0.928). The secondary outcome measure, the F1-score, was 0.608 (95% CI: 0.586-0.630) for the 12-channel montage. The overall performance of the RF models developed with a gradually reduced number of electrodes was not significantly different for any of the electrode combinations. The most contributing qEEG features for the model development were the regularity, amplitude (minimal, maximal) and the EEG Silence Ratio (ESR). All developed models struggled with distinguishing the degree of signal continuity and were unable to differentiate between identical and non-identical bursts in a burst suppression pattern.

Conclusion: The findings of this study demonstrate that the performance of a RF model remains unaffected by the utilisation of different montages with less EEG electrodes. These findings suggest that the evaluation of the EEG background pattern predominantly depends on the uniform and widespread manifestation of postanoxic encephalopathy. Future research should primarily focus on incorporating qEEG features that can further enhance the differentiation between the different categories and decreasing bias in the ground truth. Eventually, less electrodes may be used for the EEG assessment after CA.

3.1 Introduction

Accurately predicting neurological outcome following Cardiac Arrest (CA) holds significant importance in clinical practice. Not only to provide precise information to the patient's relatives, but also to prevent excessive treatment in patients suffering from severe and irreversible hypoxic ischemic brain injury, who are unlikely to achieve meaningful neurological recovery. A CA happens when all heart activity is suddenly lost, usually due to an irregular hearth rhythm, and can happen in two settings: Out of Hospital Cardiac Arrest (OHCA) and In Hospital Cardiac Arrest (IHCA). In OHCA, survival rates are often low, with a 1-year survival rate of about only 8%. [1] Survival rates for IHCA are generally slightly higher and have been increasing over the years, with reported 1-year survival rates of 13%. [2–4] If a patient reaches return of spontaneous circulation after cardiopulmonary resuscitation, patients are usually admitted to the Intensive Care Unit (ICU). Here they often suffer from postanoxic encephalopathy due to insufficient bloodflow and oxygen supply to the brain. Regarding the neurological prognosis of these patients, multiple modalities are being investigated or are already used, with the EEG being an important one. [5–7] In the Netherlands, a national guideline on prognostication in postanoxic encephalopathy came into effect in 2019, which describes several EEG background patterns associated with a poor- or good neurological outcome that should be used to guide clinical treatment. [8]

As most of the ICU staff has not been trained in the assessment of EEG signals, prognostication in postanoxic encephalopathy is a multidisciplinary effort. A trained EEG technician should be available to connect and maintain the EEG electrodes, which is a time consuming and labour intensive process. Furthermore, interpretation requires a trained clinical neurophysiologist. [9, 10] After CA, a clinical neurophysiologist usually assesses the EEG visually at 12 and 24 hours after CA, as the background patterns at these time points are validated for the neurological prognostication. [8]

One possible approach to alleviate the workload of the EEG technician involves minimising the number of electrodes used for EEG monitoring. This reduction could directly lead to a decrease in the time required for electrode attachment, as in our experience each additional electrode takes approximately an additional minute to attach. The American Clinical Neurophysiology Society (ACNS) recommends that in usual clinical recordings of EEG at least sixteen channels should be used to show the areas of the brain producing most (ab)normal electrical activity. [9, 11] Although some studies have investigated the effect of reducing the amount of electrodes on e.g. seizures and rhythmic pattern detection with promising results, [12, 13] the effect of reducing EEG electrodes at the ICU on pattern detection, interrater agreement, and intermontage agreement varies. [14–17] In postanoxic coma, there typically is a widespread diffuse cortical distribution, which might still be captured with a reduced number of EEG electrodes. Tjepkema-Cloostermans et al. (2017) showed that the reduction from 21 to 10 EEG electrodes did not affect visual EEG background pattern classification in postanoxic encephalopathy. [18] Additionally, small studies show a reduction to 8/6 electrodes may be feasible as well. [19, 20] The current relevance of this research question is evident, as demonstrated by a study published during the execution of the current study that examined visual classification based 4 electrodes. [21]

To reduce the labour-intensiveness and subjectiveness of EEG interpretation, the amount of research done on the quantitative analysis of the EEG using Artificial Intelligence (AI) techniques like ML is increasing. Recent studies are mostly aimed at automatically predicting the outcome in postanoxic coma. [22–25] Although the use of qEEG could decrease subjectivity and workload regarding the EEG reviewing process, the need for further research and standardisation of review methods before clinical implementation is evident. [26] To benefit from the possibilities of quantitative assessment while adhering to the agreed-upon definitions of the ACNS and national guidelines, it would be interesting to automatically classify the background pattern of the EEG using qEEG. Attempts to achieve this goal have not yet been made.

3.1.1 Objectives

In this retrospective study, we aimed to optimise EEG analysis and application methods to reduce the labour intensiveness of EEG monitoring in patients after CA. The main objectives of this study were:

- To develop a ML model for EEG background pattern classification in postanoxic encephalopathy
- To evaluate the effect of the reduction of the amount of EEG electrodes used for automatic EEG background classification in postanoxic encephalopathy on the model performance compared to a full montage with 13 EEG electrodes

3.2 Methods

3.2.1 Study population

All consecutive postanoxic comatose patients admitted to the ICU of the Erasmus MC, Rotterdam, between October 5th 2019 and April 25th 2023 were screened for inclusion in this study. Continuous electroencephalography (cEEG) was part of standard clinical practice and used to guide neurological prognostication. Patients were considered eligible for inclusion in this retrospective study if cEEG was initiated within 24 hours of CA and visual assessment at 24 hours after CA was available. The Medical Ethical Committee Rotterdam approved the study protocol (MEC-2021-0145).

3.2.2 EEG data acquisition and standard care

EEG data was recorded using an OSG BrainRT system (Rumst, Belgium) at a sample rate of 256 Hz. The data was recorded using Cz as a recording reference, and an analog high-pass filter at 0.1 Hz. From October 5th 2019 until December 22th 2021, 21 electrodes were used. From then on, 13 electrodes (Fp1, Fp2, F7, F8, T3, T4, T5, T6, O1, O2, C3, C4, Cz) were used after successful local evaluation of background pattern assessment with the use of fewer electrodes. Electrodes were placed according to the international 10-20 system, and efforts were made to maintain electrode impedance below 5kΩ. As per the local and national protocol, EEG recordings were started as soon as possible after admission to the ICU and continued for a minimum of 24 hours after CA. In case the patient regained consciousness or it was determined that life-supporting treatment should be discontinued, the EEG recordings were terminated earlier. As part of the standard clinical practice and neuroprotective strategy, all patients received Targeted Temperature Management (TTM) at 36 ℃ during the first 24 hours of ICU admission.

3.2.3 Ground truth

EEG background pattern was described as part of standard clinical care and prognostication after CA at the time of the EEG recording. The original visual assessment, as described by an experienced clinical neurophysiologist, was used as the ground truth in this study. In case of missing descriptions, we excluded data from this study. Based on the background pattern descriptions, we defined 9 different categories (Table 3.5). The EEG background patterns were defined based on the ACNS criteria and the national protocol for the prognosis of postanoxic coma, and some of these categories have proven to have prognostic power at either 12 or 24 hours after CA. [8, 10]

3.2.4 EEG data preprocessing

The raw EEG data as recorded in BrainRT$^{\mathrm{TM}}$ at 256 Hz was converted to an EDF+ file, and an additional event-file (.tsv) with the descriptions of the visual assessment during the time of EEG recording was generated. We used the latter file to deduce any input mentioning “24” to obtain the written visual assessment of the background pattern at 24 hours after cardiac arrest (T24). Next, we extracted the onset time, which is the duration from the beginning of the EEG recording to the T24 point in seconds. The data was validated by visually inspecting the extracted event entries.

Utilising the onset points, we selected a 30-minute epoch from -15 to +15 minutes surrounding T24 for each patient. The selected epochs consisted of the 13 electrodes that were present in all recordings (Subsection 3.2.2). Subsequently, all epochs were subjected to visual analysis to identify any bad channels or major artefactual fragments. We removed epochs containing bad channels from the analysis completely. Next, a notch filter at 50 Hz and a non-causal finite impulse response (FIR) bandpass filter with a low-pass of 0.5 Hz and a high-pass of 35 Hz were used to filter all epochs. Moreover, we implemented Independent Component Analysis (ICA) analysis to remove ECG artefacts. The filtered EEG fragments were rereferenced through common referencing with Cz set as the common reference electrode, resulting in 12 EEG channels. Before the data was split into consecutive epochs of 20 seconds with 5 seconds of overlap, we downsampled the data to 128 Hz for computational purposes. When creating the 20-second epochs, we removed all epochs that partially or fully overlapped with an annotated bad fragment from the data. The described workflow is further elaborated upon in Supplementary Material J. In addition to the visual inspection of artefacts, remaining artefactual epochs were removed based on amplitude and the total power of the Power Spectral Density (PSD) from 0.5 to 35 Hz. The maximum amplitude of all 20-second epochs was calculated, and we set a threshold at 300 μV, as physiological brain activity will not exceed this voltage. Subsequently, the threshold for the total power was set at 2000 W/Hz. All epochs exceeding these threshold were removed from further analysis. The described preprocessing steps were performed using the MNE toolbox (version 1.4.0) in Python (version 3.8). [27]

3.2.5 EEG feature analysis

For each included patient in this study, we calculated a total of 26 qEEG features. These features were first computed per epoch for each individual EEG channel. Channel values were then averaged to generate a single value per feature per epoch, which subsequently was averaged to result in a final feature value per patient. We included features from the time-, frequency-, complexity-, and connectivity domain in this study that were based on previous studies on the prognostic value of EEG in postanoxic coma in both adults as well as the pediatric population. All of the features included in the analysis are presented in Table 3.6, and a detailed description of the features is provided in Supplementary Material K.

3.2.6 Model development

For the automatic classification of EEG background pattern, we developed a RF classifier. A RF classifier is a supervised ML method that combines multiple decision trees to make a final prediction. The development of the RF model followed a systematic procedure (Figure **??**). To ensure reliable model performance, we employed a 5-fold cross-validation approach, wherein the data was stratified to maintain the distribution of the different classes in both the training and test sets. The training set consisted of 80% of the data. The optimal hyperparameters for the model were selected in a randomised search with 30 iterations for every fold in a 5-fold cross-validation of the training set (Supplementary Material L). For every optimised RF classifier, the 20% test set was used for model performance evaluation. To further evaluate the performance of this selected RF model, we repeated the the 5-fold cross-validation 20 times. The RF model development and -evaluation were performed using the Scikit-learn toolbox. [37]

Table 3.5: Electroencephalography (EEG) background patterns in postanoxic encephalopathy, used in clinical practice for the prognosis at either 12 or 24 hours after cardiac arrest. [8] Definitions based on the EEG critical care guideline of the American Clinical Neurophysiology Society (ACNS). [10] BS: Burst Suppression. GPD: Generalised Periodic Discharges.

	Background pattern	**Definition**	**Prognosis**	**Hours post-CA**
1	Continuous background pattern with normal amplitudes	>99% activity, amplitudes >20 μV	Good (12) Uncertain (24)	12/24
2	Continuous but suppressed background pattern	>99% activity, amplitudes <20 μV	Poor	24
3	Nearly continuous	1%-9% amplitudes < 10 μV	Uncertain	Uncertain
4	Discontinuous	10-49 % suppression (<10 μV) without BS and/or GPD	Uncertain	24
5	No cerebral activity, iso-electric	> 99% suppression	Poor	12/24
6	BS with non-identical bursts	Any at least four-phasic pattern (>20 μV) with a duration of ≥0.5 sec. alternated with periods of low (<10 μV) EEG activity of at least 1 sec.	Uncertain	24
7	BS with identical bursts	BS with first 500 ms identical on the eye, irrespective of amplitude or subsequent duration of bursts or inter-burst intervals	Poor	24
8	GPD on a flat background	Bilateral synchronous and symmetric periodic discharges <0.5 sec. with periods of no cerebral activity	Poor	24
9	GPD on a continuous background	Bilateral synchronous and symmetric periodic discharges <0.5 sec.	Uncertain	24

Table 3.6: Quantitative electroencephalography (EEG) features included in this study. BSR: Burst Suppression Ratio. ESR: EEG Silence Ratio. PSD: Power Spectral Density. ApEn: Approximate Entropy. TsEn: Tsallis Entropy. SpEn: Spectral Entropy. BCorrD: Bivariate Correlation. PLI: Phase Lage Index.

EEG feature		**Feature description**
Amplitude		The minimal, maximal and mean amplitude of the EEG signal
BSR		The fraction in which the amplitude of the EEG signal is $<5\ \mu$V
ESR	[28]	Intervals of suppression of >240 msecs during which the EEG signal is $<5\ \mu$V
Spikes	[29]	Waves with a high amplitude (>2.5*std of the signal amplitude) and maximum width of 70 ms
Regularity	[30]	The regularity of the amplitude of the signal
Frequency bandpower		PSD in different frequency bands
Absolute & Relative		Delta: 0.5-4 Hz Theta: 4-8 Hz Alpha: 8-12 Hz Beta: 12-30 Hz
Hjorth parameters	[31]	
Activity		The variance of a time-signal
Mobility		The standard deviation of the power spectrum
Complexity		The change in frequency and similarity to a sine wave
Entropy		
ApEn	[32]	Quantification of the unpredictability of fluctuations in a time series
TsEn	[33]	Quantification of the uncertainty of stochastic signals in the frequency domain, with non-extensive statistics
SpEn	[34]	Quantification of the uncertainty of stochastic signals in the frequency domain
BCorrD	[35]	Bivariate correlation between two signals
Coherence		Measure of the similarity between the PSD of two signals
PLI	[36]	Measure for the asymmetry of the distribution of phase differences

3.2.7 Evaluation of model performance

The performance of the RF was evaluated using different performance metrics. For the primary outcome measure, we used a OvR approach to compute the AUC-ROC. The OvR approach involves treating each of the EEG background classes as a binary classification problem, where one class is considered as "positive" and the rest of the classes as "negative", and calculating the AUC-ROC score for each individual class. A ROC curve for each of the EEG background categories was generated within each fold, and the average over the five folds was calculated. Additionally, the micro-averaged AUC-ROC was calculated to be able to evaluate the overall performance of the classifier over all categories. As secondary outcome, the F1-score was calculated for each of the 5 folds. The F1-score is the harmonic mean of precision (the accuracy of positive predictions) and recall (the ability to identify all positive samples). We used these metrics to evaluate the performance of the model as they are less sensitive to imbalanced EEG background classes.

To further evaluate the performance of the model, we generated a confusion matrix of the classification of EEG background category of all patients to compare the predictions of the algorithm with the label assigned through visual analysis. Finally, we evaluated the importance of the included features with a permutation approach to calculate the mean decrease in accuracy of the classifier after the permutation of a single feature compared to the baseline model with all features.

3.2.8 Reduction of electrodes

In this study, we calculated the EEG features used as input for the RF in different ways. Initially, the EEG features were computed based on a 12-channel montage, which was gradually reduced to 10, 8, 6, and 4 EEG channels. For the 10-channel montage, we removed C3 & C4. Subsequently, P7 & P8, F7 & F8, and O1 & O2 were removed for the 8-, 6-, and 4-channel montages respectively (Figure L.20). This enabled the computation of five unique sets of features, leading to the subsequent training of five distinct RF models, each based on a different feature input. The aim of this approach was to determine the minimum number of electrodes necessary for calculating qEEG features, while still achieving a reliable classifier. We assessed the impact of electrode reduction by utilising Analysis of Variance (ANOVA) statistics to compare the average outcome metrics across the 20 iterations of model development.

3.3 Results

3.3.1 Patient- and EEG characteristics

A total of 542 EEG recordings of postanoxic encephalopathy patients were collected in the study period, of which 358 had an EEG recording with clear description at 24 hours after CA (Supplementary Material H). After bad channel- and artefact detection, 323 patients could be included in this study (Figure H.3). Table 3.7 shows the patient- and EEG characteristics of all included patients in this study. The background pattern that was most often present based on the visual assessment was a continuous normal amplitude, followed by a discontinuous background pattern at T24. As the EEG background category “Generalised Periodic Discharges (GPD) on a flat background” was only present in 2 patients, it was decided to merge this category with “GPD on a continuous background” to a general “GPD” category. This way, the multi-class classification was based on 8 categories. There were no significant differences in patient age or -sex between the different groups.

Table 3.7: Patient- and EEG characteristics of the included patients in this study. *Groups were compared for mean age using ANalysis Of VAriance (ANOVA), and sex using a chi-squared test. No significant differences were found between groups (significance level $p<0.05$). BS: burst suppression. GPD: generalised periodic discharges.

Patient characteristics	**N. (%)**	**Mean age (±std)**	**Sex: females (%)**
	323	59.45 (±14.86)	72 (22.3%)
EEG background pattern			
Continuous normal amplitude	126 (%)	56.4 (±15.7)	29 (23.0%)
Nearly continuous	41 (%)	64.2 (±13.5)	5 (12.2%)
Discontinuous	33 (%)	65.1 (±14.1)	11 (33.3%)
BS non-identical	55 (%)	60.7 (±13.6)	11 (20.0%)
Iso-electric	24 (%)	54.8 (±16.5)	6 (25%)
BS identical	17 (%)	62.9 (±15.9)	5 (29.4%)
Low voltage	15 (%)	59.3 (±11.8)	3 (20%)
GPD	12 (%)	58.4 (±6.8)	2 (16.7%)
p-value*		0.115	0.563

3.3.2 Model performance

The OvR Receiver Operating Characteristic (ROC) curves of the five-fold cross-validation are shown in Figure 3.7. The micro-averaged AUC of the baseline model with a montage of 12 channels was 0.923 (95% CI: 0.918-0.928). The AUC of the different OvR curves varied for each category that was predicted, ranging from 0.751 (95% CI: 0.565-0.937) to 0.974 (95% CI: 0.946-1.00), with the lowest AUC for the prediction of a nearly continuous background pattern, and the highest AUC for the prediction of an isoelectric EEG background. The secondary outcome measure, the F1-score, was 0.608 (95% CI: 0.586-0.630) for the 12-channel montage. The confusion matrix of the baseline-model is shown in Figure 3.8.

3.3.3 Reduction of electrodes

The overall performance of the different RF models developed with different electrode montages was not significantly different for any of the montages, and thus the reduction of electrodes used for model development did not impact discriminating abilities (Figure 3.9 & Table 3.8).

3.3.4 Feature importance

The mean decrease of the model performance of the 12-electrode baseline model by the permutation of all included features is shown in Figure 3.10. The most contributing qEEG features for the model development were the regularity, amplitude (minimal, maximal) and the ESR. The least important features included the delta- and theta coherence, and Spectral Edge Frequency at 90% of the power spectrum (SEF90).

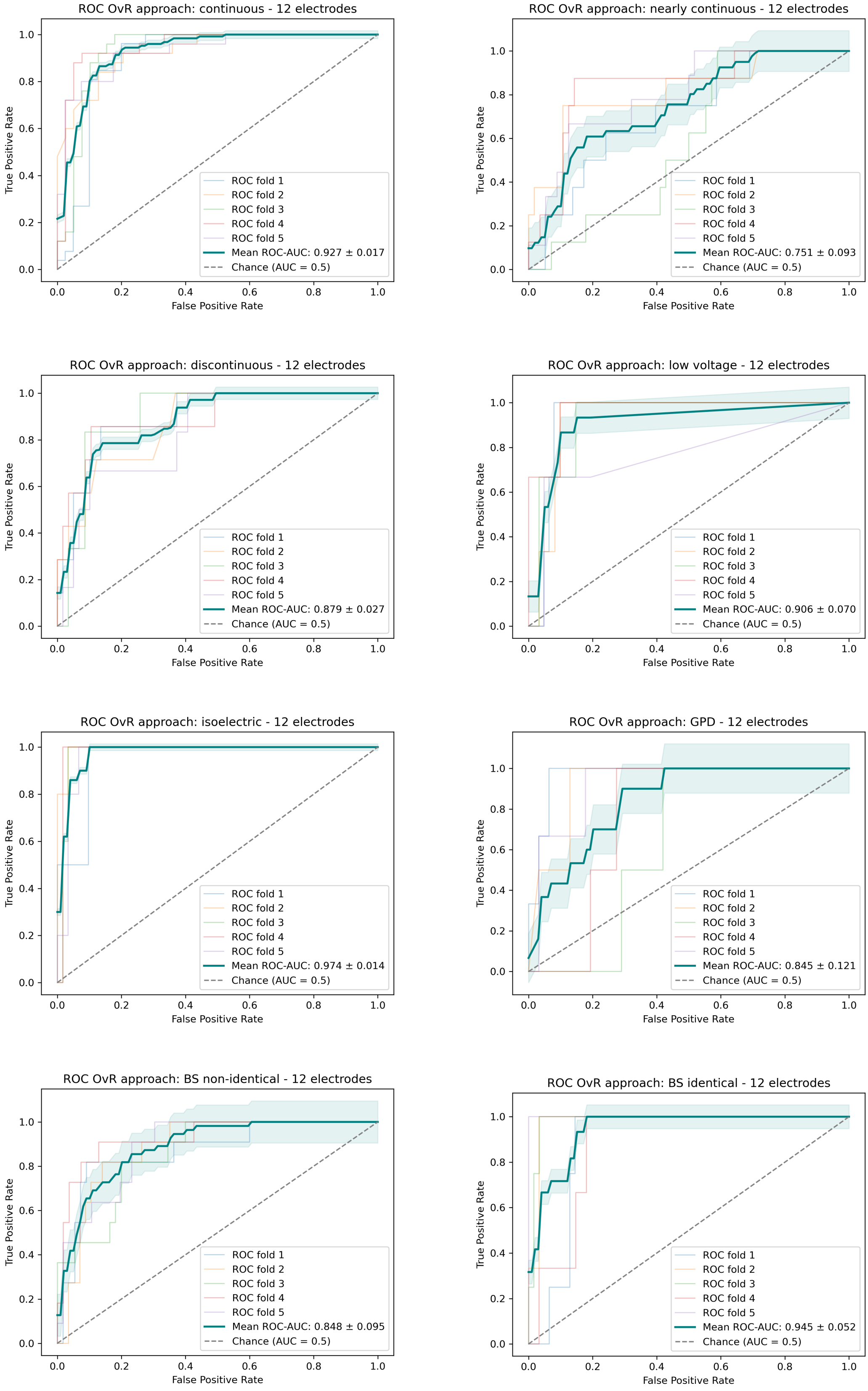
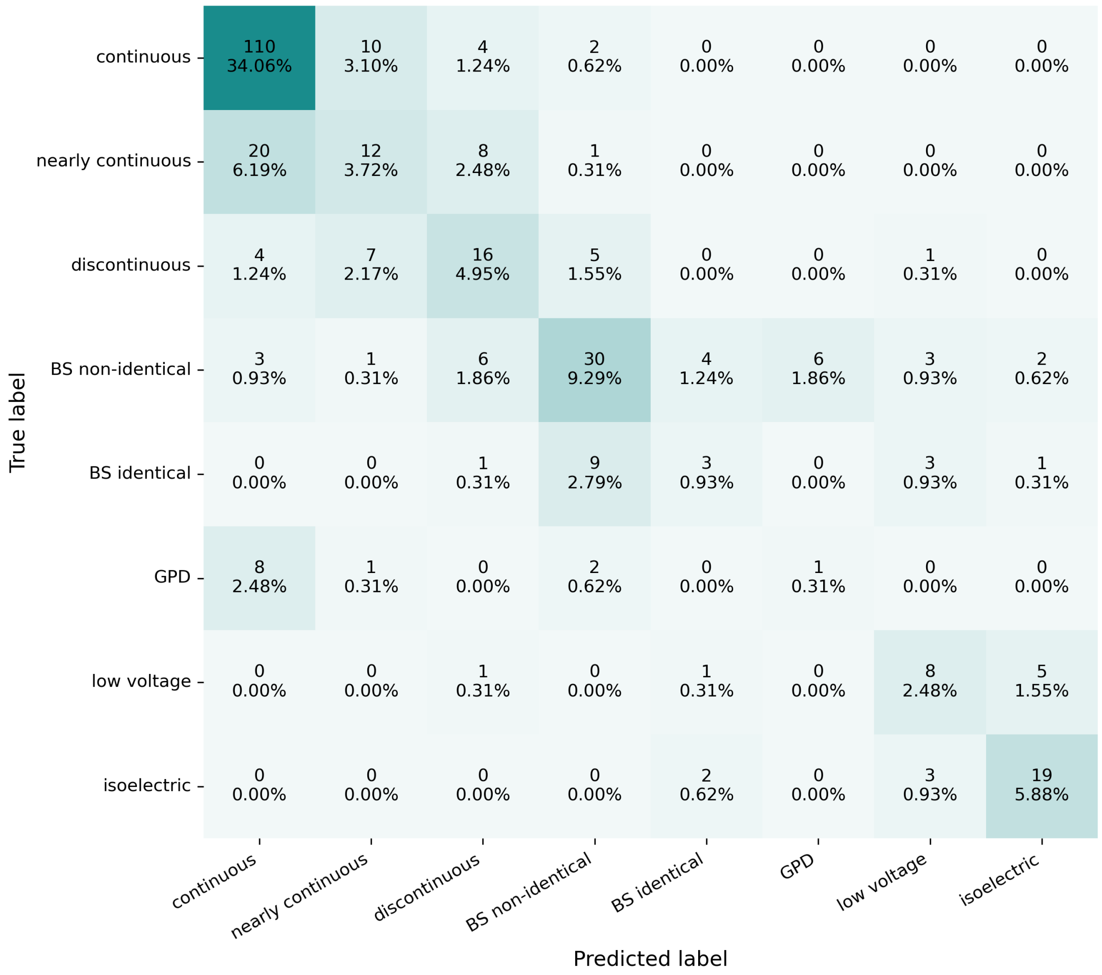


Figure 3.7: One-vs-Rest (OvR) Receiver Operating Characteristic (ROC) curves per EEG background category of a Random Forest classifier developed with input from 12 EEG electrodes. Plots were generated in a 5-fold cross-validation. The curves for all 5 folds and the mean and standard over these folds deviation are visualised.



True label \ Predicted label	continuous	nearly continuous	discontinuous	BS non-identical	BS identical	GPD	low voltage	isoelectric
continuous	110 34.06%	10 3.10%	4 1.24%	2 0.62%	0 0.00%	0 0.00%	0 0.00%	0 0.00%
nearly continuous	20 6.19%	12 3.72%	8 2.48%	1 0.31%	0 0.00%	0 0.00%	0 0.00%	0 0.00%
discontinuous	4 1.24%	7 2.17%	16 4.95%	5 1.55%	0 0.00%	0 0.00%	1 0.31%	0 0.00%
BS non-identical	3 0.93%	1 0.31%	6 1.86%	30 9.29%	4 1.24%	6 1.86%	3 0.93%	2 0.62%
BS identical	0 0.00%	0 0.00%	1 0.31%	9 2.79%	3 0.93%	0 0.00%	3 0.93%	1 0.31%
GPD	8 2.48%	1 0.31%	0 0.00%	2 0.62%	0 0.00%	1 0.31%	0 0.00%	0 0.00%
low voltage	0 0.00%	0 0.00%	1 0.31%	0 0.00%	1 0.31%	0 0.00%	8 2.48%	5 1.55%
isoelectric	0 0.00%	0 0.00%	0 0.00%	0 0.00%	2 0.62%	0 0.00%	3 0.93%	19 5.88%

Figure 3.8: Confusion matrix of the true background pattern versus the predicted background pattern of all included patient in this study. The confusion matrix was generated in a 5-fold cross-validation approach using a Random Forest classifier based on a 12-electrode montage. BS: burst suppression. GPD: Generalised Periodic Discharges

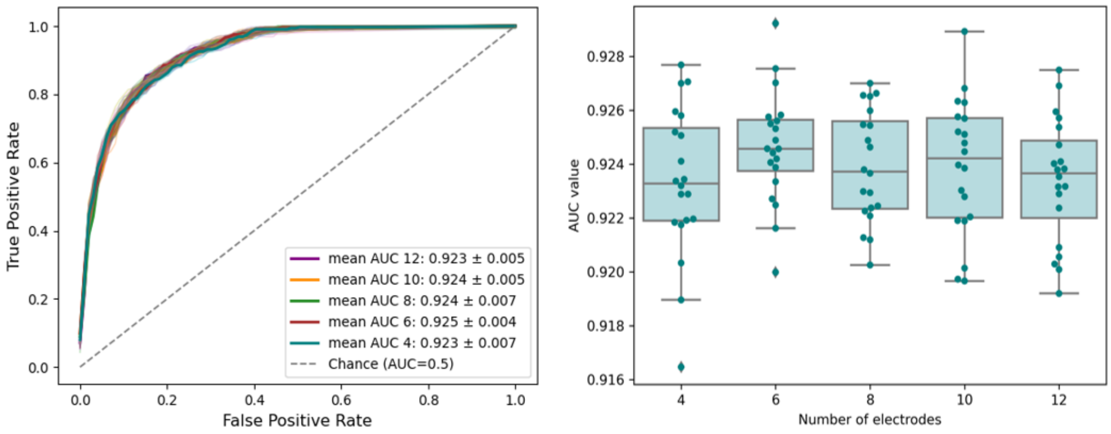


Figure 3.9: Comparison of micro-averaged Area Under the Curve (AUC) values over 20 repeats of a 5-fold cross-validated Random Forest classifier for the prediction of EEG background pattern using 12, 10, 8, 6, and 4 EEG electrodes.

Table 3.8: Comparison of outcome measures for 12-, 10-, 8-, 6-, and 4-channel mongtages used EEG background pattern prediction. The mean values over 20 folds of model development are presented. *p-value significance level of ANalysis Of VAriance (ANOVA) statistics: <0.05 AUC: Area Under the Curve. BS: Burst suppression. GPD: generalised periodic discharges.

Outcome measures	Number of EEG channels					p-value*
	12	10	8	6	4	
Micro-averaged AUC	0.923	0.924	0.924	0.925	0.923	0.279
Continuous	0.928	0.930	0.931	0.933	0.928	0.502
Nearly continuous	0.746	0.757	0.755	0.760	0.779	0.986
Discontinuous	0.884	0.888	0.891	0.891	0.893	0.497
BS non-identical	0.888	0.889	0.888	0.892	0.867	0.983
Iso-electric	0.976	0.974	0.976	0.975	0.978	0.112
BS identical	0.944	0.946	0.951	0.938	0.944	0.391
Low voltage	0.915	0.906	0.909	0.906	0.912	0.328
GPD	0.826	0.838	0.835	0.848	0.861	0.948
F1-score	0.608	0.606	0.609	0.608	0.628	0.652

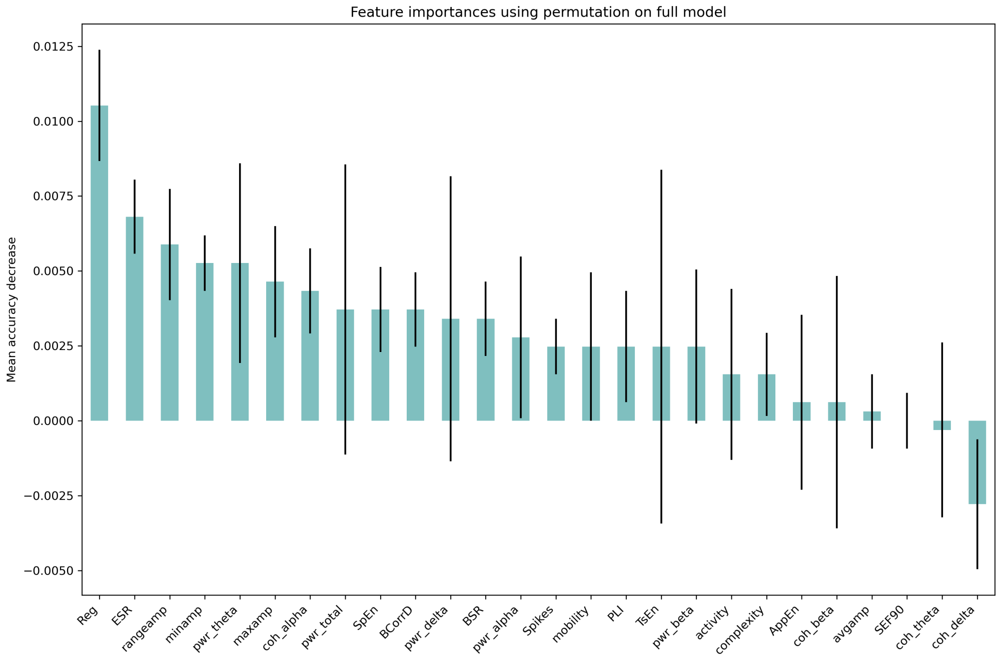


Figure 3.10: Feature importance of the Random Forest classifier developed with input from 12-channel EEG. Feature importances were generated using a permutation approach on the developed model and evaluating the loss in accuracy after removing each of the features.

3.4 Discussion

The aims of this study were to develop a ML model for the automatic EEG background pattern classification in postanoxic encephalopathy and additionally evaluate the effect of reducing the number of EEG channels used for feature calculation on model performance. For this purpose, we included EEG recordings of 327 patients with postanoxic encephalopathy in this study. The baseline model with 12 EEG channels exhibited good performance (AUC: 0.923). Furthermore, the findings of this study demonstrate that regardless of the specific EEG electrodes employed, a well-performing random forest (RF) model can be developed.

A reduced number of EEG electrodes

In this study, we showed that the performance of the developed models remains unaffected by the utilisation of a varying number of electrodes. Although this was the first study to evaluate the effect of a reduced number of electrodes on automatic EEG background pattern classification, results are in accordance with similar studies on the visual assessment of EEG background pattern. [18–21, 38] These findings suggest that the evaluation of the EEG background pattern predominantly depends on the uniform and widespread manifestation of postanoxic encephalopathy. Consequently, for neuroprognostication purposes in this particular disease, a reduced channel montage appears to be a viable option. However, when it comes to neuromonitoring where localised brain activity holds greater significance, specifically in cases involving epileptic abnormalities, it is still advised to use a complete montage. [11]

Overall model performance

While the developed models exhibited satisfactory performance overall, they encountered difficulty in distinguishing between the EEG background categories continuous, nearly continuous, and discontinuous. Some of this difficulty can be attributed to interrater variability. Although the background categories in this study were defined based on the ACNS criteria, it appears that these definitions are not always strictly adhered to in clinical practice. Therefore, it is likely that part of the ground truth in this study was not accurate, which could have affected the model's ability to correctly identify these patterns.

Two other categories that were often misclassified were Burst Suppression (BS) with- and without identical bursts. In clinical practice, there is often disagreement on the degree of similarity of bursts, so again the ground truth might not always be "correct", as only one clinical neurophysiologist visually assessed the EEG recordings. However, a more probable explanation for this misclassification is the absence of any features in the study that capture the degree of signal similarity. Furthermore, we computed the features per 20-second epoch, but the mean value of these epochs was employed during the final model development. Additional features isolating bursts in a BS pattern and comparing the properties of multiple bursts within the same recording could increase the discriminative ability of ML models. It is desirable to establish a quantitative definition for identical bursts as this would mitigate interrater variability and could assist in the visual assessment of the EEG background pattern. Furthermore, this could enhance the accuracy of the automatic classification process.

A last category that was often misclassified was the GPD. The classification of GPDs presented the highest number of errors in the developed baseline model. One possible explanation for this observation is that GPDs can manifest on either a continuous or a flat background. However, due to their low incidence within the study sample, we combined these distinct categories. As a result, the merged category possesses a challenge for accurate classification. Furthermore, barely any of the included features capture epileptic activity, rather they are aimed more at differences in signal amplitude and frequency characteristics. Another aspect to consider is the difference between non-identical bursts and GPDs. Although the definitions of these two patterns differ, there is gray area where discharges within the same EEG sometimes classify as GPDs and other times as non-identical bursts. Due to this ambiguity, there is a potential occurrence of misclassifications in the visual EEG assessment.

Quantitative EEG features

The most important features for all developed models included the ESR, Burst Suppression Ratio (BSR), regularity and amplitude of the signal. The ESR quantifies the ratio of suppression in EEG activity. This feature is close to 0 in a continuous signal and close to 1 in a highly suppressed EEG, explaining why this feature was important in the model. Similarly, the regularity feature of EEG was developed specifically to distinguish between a continuous or BS pattern. A signal with a constant amplitude has a regularity of 1, whereas a highly suppressed signal with high-amplitude bursts has a value close to 0. The shorter the period of suppression, the higher the regularity. [30] Despite the plausible explanations for the emergence of the most important features, there is a possibility of bias in their importance. This arises from the fact that features distinguishing the largest groups also tend to exhibit the largest decrease in accuracy. In the case of equal distribution among different categories, it is conceivable that other features could emerge as more effective in distinguishing between all EEG background categories. Such features would hold greater value and applicability in clinical practice.

3.4.1 Study strengths & limitations

One strength of this study was the inclusion of a large patient group and the minimal exclusion criteria, as this provides a comprehensive representation of clinical practice. One observation we noted is the infrequency of certain EEG background categories, which posed challenges in developing a robust model. However, to limit the influence of this background pattern imbalance, we set a "balanced" parameter in the RF classifier and the metrics used to evaluate model performance (AUC-ROC, F1-score) are known to handle imbalances in data well. Furthermore, alongside the imbalance in background categories, there is a possibility of bias in the definitions itself. It is well-established that there is substantial interrater variability when it comes to assessing EEG recordings, [39] and that the variability can be reduced by using the ACNS criteria. [40] In this study, we determined the ground truth based on the assessment of a resident with supervision of an experienced clinical neurophysiologist. However, we observed that the ACNS criteria were not always strictly followed. Hence, it is important to acknowledge that certain misclassifications made by the model could potentially be attributed to inherent variability in the assessment process rather than being definitive "incorrect" classifications.

Given that the primary objective of this study was to assess the impact of electrode reduction, efforts were made to minimise the influence of other factors. Therefore, we selected a re-referencing method that would not change for the different number of electrodes. The Cz electrode, which captures brain activity, was used as a reference. The choice of the reference method employed in this study may have exerted a significant influence on the results. It is generally preferred to utilise a reference electrode that is as electrically neutral as possible, which was not possible in this retrospective study. A common way to limit the influence of noise is by using an average reference. However, the average reference would change for every new montage with reduced electrodes and might not have had its desired effect when using only a limited set of electrodes. Future analyses could provide valuable insights by exploring different reference methods (e.g., average referencing, bipolar referencing) and their effect on model performance, rather than solely focusing on the number of electrodes utilised.

Another strength of this study lies in the deliberate choice to prioritise the transparency and comprehensibility of the results, and thus developing a RF model instead of opting for different ML models. While this decision may introduce certain limitations, such as the potential impact of artefacts on the predictive capabilities of RF models, [41] we aimed to maintain the explainability of the developed models, enabling healthcare professionals to effectively understand and utilise the outcomes of the models in the future.

An important limitation of this study was the lack of an external validation set to independently test the model's performance. If the model were to be further developed for automated assessment of background patterns, it is necessary to validate the results on an external dataset. However, we expect that the effects of the reduction of electrodes on model performance as presented in this study are generalisable, irrespective of the dataset used, as they are in line with the current literature on visual EEG assessment.

Furthermore, the precise timing of the extraction of 30-minute epochs remains uncertain, thereby raising concerns regarding their accuracy. The selection of epochs was based on the visual description of the background pattern, specifically referring to T24. However, it is plausible that this moment does not align precisely with the actual occurrence of T24. Particularly when the T24 moment occurred during the night, it might be possible the descriptions were placed the following morning. In an attempt to minimise errors, we visually evaluated the extracted descriptions. Nonetheless, as the EEG background pattern in postanoxic encephalopathy can evolve over time, it might be possible some of the fragments had a description not matching the background pattern of the extracted 30-minute epoch.

3.4.2 Future research

Future research should primarily focus on incorporating additional EEG features that can further enhance the differentiation between the different categories. This could include measures such as cross-correlation to distinguish between identical and non-identical bursts. [42] Furthermore, as we currently only present the effect of the reduction to specific EEG montages, no definitive conclusions on the relevance of specific electrodes can be drawn yet. In addition, it is advised to apply stricter adherence to the ACNS criteria when labeling the ground truth, so that the model can learn more effectively. [10]

In future research, it would be interesting to explore the systematic removal of electrodes using a permutation analysis, similar to the analysis of feature importances conducted in this study. Furthermore, the RF ideally has even better discriminative power before making any assertions regarding the impact of electrode reduction. It is possible that any additional features are dependent on the number of electrodes utilised. Therefore, it is crucial to improve the model further, potentially by incorporating more features, before evaluating the true effect of electrode reduction. Additionally, the number of electrodes used for EEG assessment is not the only relevant technical consideration. Methods for preprocessing, sampling frequency, duration of the epoch around T24 used for assessment, rereferencing methods, and filtering steps are all factors that should be investigated in future research to potentially improve the labour-intensive aspects of applying, maintaining, and evaluating EEG. Moreover, some of these factors could potentially contribute to more efficient data storage, computational speed, and energy consumption.

A significant part of the patients, nearly half of them, had to be excluded from the analysis due to the inability to extract the T24 moment from the event entries. The original database indicated that there should be at least 462 EEG recordings available at T24. Consequently, there remains a substantial amount of data from which a ML model could potentially learn. In future studies, incorporating these additional patients into the analysis could augment the sample size across all categories and potentially enhance the overall performance of the developed models.

Potential confounders that were not accounted for in the analysis include age, gender, medication, and underlying organ failure, such as renal and hepatic failure. While these variables may not have a direct impact on the classification of background patterns, it is important to acknowledge their potential influence on (measurable) brain activity. Ideally, the model should be capable of considering these factors and adjusting feature thresholds accordingly. By incorporating this information, the model could further enhance its performance and provide a more comprehensive assessment of the EEG recordings.

3.4.3 Clinical relevance

In order to successfully implement algorithms like the one developed in this study, it is imperative to assess the level of trust that clinical neurophysiologists and intensivists have in AI-driven healthcare, as well as in the utilisation of a reduced number of EEG electrodes. In clinical practice, even with a full electrode montage, determining the prognosis of a patient with postanoxic encephalopathy can be challenging, sometimes even lacking a definitive conclusion. Consequently, we believe that the option to review raw EEG recordings and to increase the number of electrodes used should always be available in cases of uncertainty. Nevertheless, with the suggested model refinement, we believe that AI has the potential to assist intensivists and clinical neurophysiologists in neuroprognostication following CA, thereby reducing the burden of EEG assessment. Furthermore, utilising a reduced number of electrodes, even with potentially less precise localisation, can still yield sufficiently accurate recordings, leading to a less labour-intensive application process for EEG technicians. This, in turn, has the potential to streamline workflow and improve efficiency in EEG analysis.

3.4.4 Conclusions

In this study, we showed that a feasible RF classifier for the automatic EEG background pattern assessment can be developed, independent of the amount of EEG electrodes used. However, not all patterns can be correctly identified yet, and future research should primarily focus on incorporating EEG features that can further enhance the differentiation between the different categories. Eventually, less electrodes may be used for the EEG assessment after CA, reducing the workload for both EEG technicians and clinical neurophysiologists.

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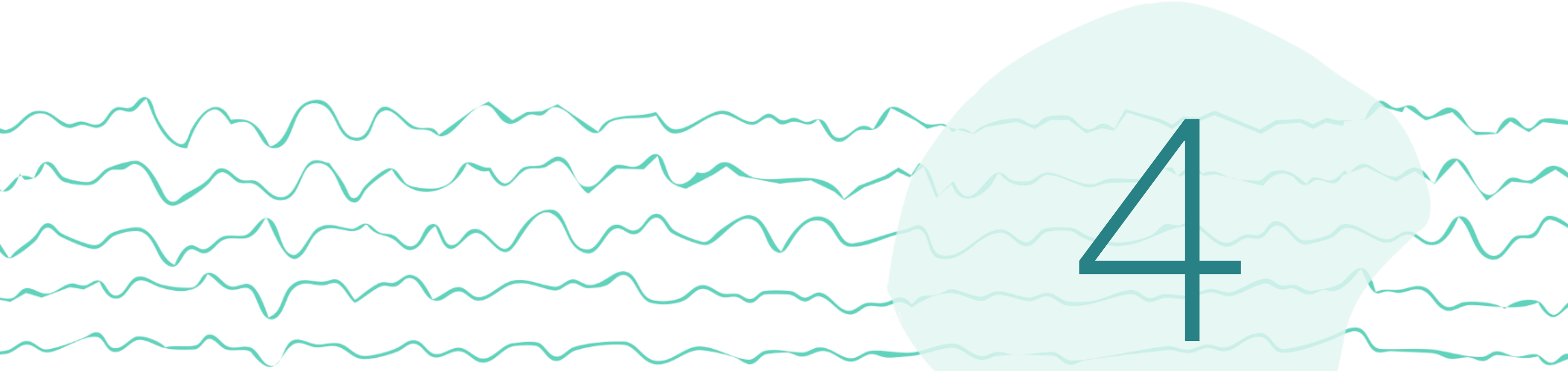

4

FUTURE PERSPECTIVES AND CONCLUSIONS

A considerable number of critically ill patients suffer from primary or secondary brain injury, requiring monitoring of this vital organ. However, continuous neuromonitoring in the Intensive Care Unit (ICU) is not yet common clinical practice. Nevertheless, one frequently used technique for continuous neuromonitoring, which has the potential to enhance the diagnosis, prognosis, and understanding of the brain's condition in critically ill patients is the electroencephalography (EEG). However, the labour-intensive nature of applying, maintaining, and interpreting EEG hinders its optimal utilisation. In preparation of a project aimed at improving the EEG monitoring workflow at the Erasmus MC, the objective of this thesis was to identify both the logistical and technical requirements for optimal monitoring, specifically exploring strategies to reduce the labour-intensive nature of EEG application and interpretation, thereby enhancing overall efficiency.

In **Chapter 2** of this thesis, we conducted a qualitative study to map out the current workflow and identify barriers and facilitators for change in the EEG monitoring workflow at the ICU. For this purpose, we interviewed several healthcare- and research professionals to gather their preferences regarding EEG monitoring in critically ill patients. Two significant findings emerged from these conversations: the desire to simplify the application process for the EEG technician, and the need for automated tools to assist in EEG interpretation, potentially benefiting the clinical neurophysiologist as well as the intensivist. Therefore, in **Chapter 3**, we explored the development of a Machine Learning (ML) model for automated assessment of the EEG background pattern in postanoxic encephalopathy; the most common indication for EEG monitoring in current clinical practice. Furthermore, we evaluated the feasibility of using a reduced number of EEG electrodes for this analysis to determine if it could still yield a robust model. Hence, this thesis examined the prerequisites for EEG monitoring in the ICU, encompassing logistical considerations, as well as technical requirements.

4.1 Future perspectives

The main logistical requirements have been identified, and we have demonstrated that the automated assessment of the EEG background pattern is not affected by the number of electrodes used as input. This indicates that in the future, fewer electrodes could be used. Does this mean that the implementation of a new workflow for EEG monitoring in the ICU at Erasmus MC can start immediately? The short answer, as is often the case in scientific research, is no, not yet. There is still much more that can and should be explored. Alkhachroum et al. (2022) suggest that the following key factors should be considered when developing an institutional protocol for the EEG monitoring at the ICU: i) what ICU EEG indications can the centre support; ii) what patient population is and should be monitored, and, iii) what is the local context (number of available technicians, available EEG reviewers, review frequency, and other workflow-related factors). [1] While we considered all these factors, and the presented findings provide valuable insights and pave the way for potential improvements in EEG monitoring, further investigation and validation is necessary before implementing a new workflow.

Although the point where automated tools can fully replace the assessment of the EEG background pattern has not been reached yet, the results presented in Chapter 3 demonstrate the potential to monitor brain activity with fewer electrodes in the most commonly monitored indication; postanoxic encephalopathy. This finding is supported by literature on the visual assessment of EEG background pattern with a reduced electrode-set. [2–6] The presented results imply that fully accurate placement of electrodes may not be necessary for assessment in postanoxic encephalopathy, which could potentially relieve EEG technicians from some of their labour. In the near future, it may even be possible to train nurses in this specific indication to apply the EEG with a limited number of electrodes in these indications. [7] This would resemble the situation in the Pediatric Intensive Care Unit (PICU) at Erasmus MC, where nurses themselves apply the amplitude-integrated electroencephalography (aEEG), for which 4 EEG electrodes are used. Although experience shows that the quality of the EEG may potentially be slightly compromised in such cases, in postanoxic encephalopathy this may be less critical. In the event that this approach is implemented, an EEG technician could always add additional electrodes to a full montage if the limited montage does not provide sufficient information or if there are concerns about the presence of epileptiform abnormalities in the EEG, as recommended by the ACNS. [8, 9]

In a hypothetical scenario, it would be ideal if there was no need for individual electrode placement and instead, an EEG cap or a system specifically designed for the ICU (such as the Brainstatus [10] or CerebAir [11, 12]) could be utilised by ICU nurses at 24 hours after Cardiac Arrest (CA). In this scenario, the need for the involvement of an EEG technician would be omitted. With an integrated tool, the background pattern could be automatically assessed, accompanied by a certainty score. In cases where the score is low, a clinical neurophysiologist would review the EEG background pattern. If there is uncertainty regarding the background pattern, an EEG technician could apply more precise electrodes, allowing for more accurate monitoring of the patient. The described workflow would reduce the labour intensity involved in applying EEG and potentially create availability for EEG technicians to monitor other critically ill patients who currently receive limited to no monitoring of the brain.

When considering which patients to prioritise for EEG monitoring, careful thought is necessary. It would be essential to identify patient populations where EEG monitoring can provide valuable insights and impact clinical decision-making. A major concern raised by healthcare professionals during the qualitative study (Chapter 2) was the added value of EEG monitoring. Apart from the existing benefits, what additional insights can be gained from EEG? Does extra monitoring lead to overdiagnosis? Can EEG monitoring lead to better patient outcomes? To answer these questions, conducting one or more prospective studies with well-defined patient groups and clear research questions is necessary. One indication that gathered significant interest was the early detection of ischemia in cases of hemorrhage, infarction, and/or during Veno-Arterial ExtraCorporeal Membrane Oxygenation (VA-ECMO) treatment. By defining a specific patient population and randomising into a controlled trial where some patients receive EEG monitoring while others do not, it can be determined whether monitoring these patients leads to earlier detection of ischemia and improved outcomes. Another group of interest was patients with elevated Intracranial Pressure (ICP). In a clinical study, EEG could be simultaneously applied alongside an ICP monitor to investigate whether changes in the EEG correlate with changes in invasively measured ICP, a theory supported by some case studies. [13–16]

However, before these scenarios can be implemented, we believe there are some technical and logistical requirements that need further consideration. This study primarily focused on one important aspect of the technical considerations, namely the number of electrodes used. Nonetheless, other technical factors such as referencing techniques, sample frequency, duration of EEG epochs, and filtering settings are also crucial to investigate. Furthermore, the qualitative research performed as part of this thesis revealed that interdepartmental collaboration is one of the key factors to success. In line with this, exchanging knowledge between different hospitals is deemed highly valuable. Therefore, it is recommended to conduct visits to the CN departments and ICUs of other (academic) hospitals to assess the local workflow and equipment arrangements. These visits will contribute to the optimal development of an implementation plan.

By exploring the minimum technical requirements, the impact of the increasing use of AI in healthcare, and more broadly, can be mitigated. It is becoming increasingly evident that data gathering, data storage and the development and training of Artificial Intelligence (AI) models consumes substantial energy and impacts the environment. [17, 18] Therefore, it is important to optimise and streamline the technical aspects of EEG monitoring to minimise unnecessary resource utilisation.

Furthermore, with healthcare costs continuing to rise, it is crucial to be mindful of avoiding further escalation in expenditure. Automation of certain aspects of healthcare could play a significant role in addressing this concern. [19] However, increasing the number of patients monitored has the potential to increase costs, while the effect on patient outcomes has not been established yet. Therefore, it is essential to consider the cost-effectiveness of EEG monitoring in the critically ill in future studies. Conducting health economic analyses can provide valuable insights into the economic implications of expanding EEG monitoring in the ICU.

Nonetheless, by implementing the findings of these studies into practice, it becomes possible to attain overall health benefits for critically ill patients and improve cost-effectiveness. Improved prognostic abilities for critically ill patients enable more informed decisions about the appropriate care to be administered to each patient. The availability of additional monitoring capacity due to the use of fewer electrodes allows for the optimisation of treatment plans for these patients, ultimately leading to improved overall healthcare.

4.2 Conclusions

In this thesis, we have demonstrated the potential for change in the EEG monitoring workflow at the ICU of the Erasmus MC, indicating that there is an opportunity to work towards more effective and efficient neuromonitoring. We should take into consideration:

- EEG monitoring at the ICU in general was perceived as having high potential in influencing clinical management and improving healthcare.
- Significant attention should be directed towards reducing the workload of healthcare providers involved before the current workflow can be expanded.
- Reducing the number of EEG electrodes for the prognosis in postanoxic encephalopathy and automating the assessment of EEG background patterns have the potential to alleviate the workload for EEG technicians and clinical neurophysiologists, while retaining important information in the EEG.
- Effective interdepartmental collaboration between the department of clinical neurophysiology, the department of neurology, and the ICU will make a difference in improving the ability to monitor the brain of critically ill patients, thereby creating opportunities to improve patient outcomes.

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SUPPLEMENTARY MATERIALS

A Interview guide

Interviews were conducted in the Dutch language.

Introductie

In dit interview bespreken we het proces omtrent neuromonitoring middels EEG op de IC volwassenen binnen het Erasmus MC. Waarom graag deze persoon/groep interviewen? Met sleutelpersoon eerst de vragen ‘oefenen’, daarna nog stilstaan bij eventuele aanvullende vragen. Het gaat om een vrijwillige deelname, er wordt gevraagd om toestemming voor opname van het interview. Na transcriptie worden de audiofragmenten verwijderd en naam van de respondent wordt nergens genoemd. Het interview zal 30 tot 45 minuten duren. Het interview bestaat uit drie onderdelen, namelijk: een algemeen deel over de omtrent neuromonitoring op de IC en een tweede deel over de implementatie van nieuwe EEG monitoring op de IC.

Deel 1: Algemeen

- Wat is je functie en hoe lang oefen je deze functie al uit? [loopbaan/ambities, motivatie]
- Als er een EEG op de IC nodig is, wat is jouw rol dan? [waar in de keten, hoe lang bezig, frequentie, met welke andere betrokkenen in direct contact? Werkbelasting?]
- Vanuit jouw perspectief: wie zijn er betrokken bij het gehele proces? [belang van deze personen]
- Hoe ervaar je de huidige workflow omtrent monitoring? [aanvragen, efficiëntie, haalbaarheid]
- Is er volgens jou toegevoegde waarde van EEG monitoring op de IC en wat is die waarde dan? [motivatie, functie, potentie]
- Welke indicaties komen nu door de triage heen? [weigeringen, welke vraagstellingen zou je eigenlijk wel willen monitoren?]
- Welke patiëntgroepen zouden we idealiter allemaal monitoren middels EEG op de IC? [motivatie, indicatie]
- Gebruiken jullie kwantitatieve analyse van het EEG?

Deel 2: implementatie van nieuwe EEG monitoring

Verdere uitleg over doel van mijn project: in kaart brengen van de huidige workflow, EEG technische voorwaarden en bevorderende en belemmerende factoren met het doel om de huidige workflow te verbeteren indien dit nodig blijkt en in de toekomst bij meer patiëntgroepen op de IC te kunnen monitoren.

- “Er is een plan om met nieuwe apparatuur en in de toekomst wellicht meer te gaan monitoren middels EEG op de IC, met als doel uiteindelijk effectiever te kunnen monitoren” Wat zijn je eerste gedachten hierbij? [toegevoegde waarde, motivatie, verandering, bereidheid]
- Zou een dergelijke verandering passen in de huidige workflow? [Hoe zie je je eigen rol wanneer we dit in praktijk willen brengen? Wat zou moeten veranderen?]
- Je noemde net al een aantal van je eerste gedachtes... Aanvullend hierop, wat zie je als bevorderende en belemmerende factoren? [waarom, frequentie, oplossing]
- Als er nieuwe apparatuur komt om meer te gaan monitoren, waar moet deze apparatuur volgens jou dan aan voldoen? [werkbaarheid, specificaties, kosten]
- Wat zie je als belangrijkste punten waarop we moeten focussen voor een geslaagde implementatie?
- Wie zou er getraind moeten worden en wie zou er moeten trainen om de implementatie te laten slagen? [capaciteit]

Controleren of alle constructen van het CFIR model voldoende zijn nagelopen.

- Innovation Characteristics
  - In hoeverre zou je ervaring op willen doen met nieuwe apparatuur voordat je het vertrouwt? [pilot, mogelijkheden]
  - EEG vergeleken met andere neuromonitoring methodes [EEG of andere optie?]
- Outer Setting
  - Hoe schat je de slagingskans van deze implementatie? [Binnen EMC, IC, KNF, financieel, politiek]
  - Zijn er bepaalde speerpunten binnen de afdeling en sluit dit hier bij aan? [prioriteit, andere projecten]
- Inner Setting
  - Hoe zie je de cultuur en de samenwerking tussen we verschillende afdelingen?
  - Hoe is de infrastructuur geregeld? Zouden er grote dingen moeten veranderen voor deze implementatie? [communicatie, protocol, ruimte]
- Individual Characteristics
  - Als het goed is besproken bij eerdere vragen, eventueel nog verder uitvragen.

Hiermee is een einde gekomen aan het interview. Ik kijk nog even of ik iets vergeten ben te vragen. Zijn er nog dingen die je zelf graag zou bespreken? Terugkoppeling over de resultaten volgt in de loop van mijn project.

B Codebook

In this supplementary material, the codebooks that were used for the analysis of the data of the qualitative study in Chapter 2 are provided. We developed these codebooks based on 23 of the constructs of the Consolidated Framework for Implementation Research (CFIR) in the Dutch language.

Table B.1: Codebook of workflow

Dimensies	**Aspect: definitie** Code: subaspect (deductief/inductief) - Voorbeeld
1. Workflow	**A. Logistics**
	Logistics: De logistieke aspecten die van belang zijn bij een potentiële indicatie voor neuromonitoring (deductief) - De neuroloog komt in consult om de patient te beoordelen - De KNF wordt gebeld voor een aanvraag voor een LEM op de IC **Efficiency**: Hoe efficient de huidige workflow verloopt (deductief) - Er wordt dubbel werk gedaan **Logistic wishes**: de ideeen en wensen die er zijn als het gaat om logistiek (inductief)
	B. Responsibilities
	Patient visit: de verantwoordelijkheden per functie als het gaat om het fysiek beoordelen van een patiënt (deductief) - De neuroloog doet neurologisch onderzoek op de IC **Online**: de verantwoordelijkheden per functie als het gaat om het online beoordelen van het EEG van een patiënt (deductief) - De KNF AIOS beoordeelt eens per uur de EEG registratie op de computer **Administration**: wie moet wat rapporteren in het elektronisch patiëntendossier (deductief) - De IC arts rapporteert de algemene indruk van de patient in het elektronisch patientendossier
	C. Workload
	Pressure: De werkdruk die wordt ervaren door het betrokken personeel(deductief) - De KNF artsen hebben het erg druk en hebben weinig ruimte voor extra taken **Working hours**: De uren die besteed worden aan bepaalde taken(deductief) - De laborant spendeert ongeveer 1 uur aan het proces dat komt kijken bij een LEM op de IC
2. Collaboration	**D. Communication**
	Communication: Hoe de verschillende betrokken afdelingen en functies onderling met elkaar communiceren (deductief) - de KNF en IC communiceren niet direct met elkaar, alleen indirect via de neurologie
	E. Efficiency
	Efficiency: Hoe efficiënt de samenwerking tussen de betrokken afdelingen en functies gaat (deductief) - Door alle overlegmomenten kan het soms meerdere uren duren voordat een advies ook echt uitgevoerd wordt
3. Indications	**F. Clinical practice**
	Clinical practice: voor welke indicaties wordt er in de huidige situatie een EEG aangesloten op de IC? (deductief) - patiënten na een OHCA in een postanoxisch coma krijgen standaard een EEG voor de eerste 24 uur na hartstilstand
	G. Research
	Research: bij welke patiënten/voor welke indicaties zou een EEG gemaakt kunnen worden in onderzoeksverband? (deductief) - Het EEG zou gebruikt kunnen worden om een hersenbloeding tijdig te detecteren door asymmetrie tussen de linker- en rechterhersenhelft te detecteren op het EEG **Research wishes**: de manier waarop wetenschappelijk onderzoek uitgevoerd zou kunnen worden (inductief)

4. Requirements	**H. Current practice**
	Current practice: Welke apparatuur wordt op dit moment gebruikt voor EEG monitoring op de IC? (deductief) - OSG BrainRT wordt gebruikt om de EEG registratie te beoordelen
	I. New equipment
	New equipment: Waar zou nieuwe EEG apparatuur aan moeten voldoen? (deductief) - De aan te schaffen EEG caps moeten aangesloten kunnen worden op de huidige hardware
	J. Research
	Research: Waar zou EEG apparatuur aan moeten voldoen om relevante onderzoeksvragen te kunnen beantwoorden? (deductief) - Om onderzoek te doen naar functionele connectiviteit zou je idealiter high-density EEG gebruiken
5. Modalities	**K. Neuromonitoring modalities**
	Evidence based modalities: Welke apparatuur wordt naast EEG nog meer gebruikt voor neuromonitoring en wat zijn de verschillen met het EEG? (deductief) - Bij patiënten met (risico op) hoge druk na een neurotrauma wordt een ICP meter gebruikt om de hersendruk te monitoren **Research modalities**: Welke modaliteiten zouden in onderzoeksverband gebruikt kunnen worden om de hersenfunctie te monitoren? (deductief) - met functional Ultrasound kun je de bloedflow in de hersenen visualiseren
	L. Out-of-the-box
	Out-of-the-box: welke modaliteiten zou je kunnen ontwikkelen of gebruiken om de hersenfunctie te monitoren? (deductief) - Met een camera op de pupillen zou je links-rechtsverschil potentieel kunnen detecteren

Table B.2: Codebook barriers & facilitators

Dimensies	Aspect: definitie Code: subaspect (deductief/inductief) +/- Voorbeeld facilitator/barrier
1. Innovation characteristics	**A. Relative Advantage**
	Relative Advantage: EEG is beter dan andere beschikbare methodes die momenteel beschikbaar zijn om de hersenfunctie te monitoren óf dan geen methode (deductief) + Het EEG geeft een real-time weergave van de hersenactiviteit, wat andere neuromonitoring modaliteiten niet kunnen - Het EEG zit relatief meer in de weg tijdens de verzorging van de patient dan een ICP meter **Clinical Practice**: EEG monitoring kan effect hebben op de klinische besluitvorming en behandelmogelijkheden, heeft directe consequenties in de klinische praktijk (inductief) + Het EEG bij pentobarbitalcoma wordt gebruikt om sedatiediepte in te stellen - Als we gaan monitoren bij hersenbloedingen, worden er in eerste instantie geen klinische consequenties aan verbonden en zal dit voornamelijk in het verband van onderzoek zijn
	B. Triability
	Triability: De nieuwe EEG caps kunnen getest worden in de vorm van een pilot-studie op een kleine schaal en de gevolgen van eerste implementatiestappen zijn niet blijvend (deductief) + Voor de implementatie kunnen eerst demomodellen van de apparatuur aangevraagd worden bij de fabrikant - Een pilot kan in eerste instantie alleen bij gezonde vrijwilligers worden uitgevoerd
	C. Complexity
	Complexity: Het EEG is complex, hetgeen kan worden weerspiegeld in de omvang en/of de aard en het aantal verbindingen en stappen (deductief) + Het EEG kan complexe netwerken binnen het brein identificeren - De interpretatie van het EEG vergt getraind en ervaren personeel **Practical**: Het EEG is aan te brengen bij IC patiënten en verstoort niet bij de verzorging van patiënten (inductief) + EEG caps zijn niet zwaar en belemmeren de bewegingsvrijheid van de patiënt niet - Patiënten met een EEG cap kunnen niet op hun hoofd gewassen worden
2. Outer setting	**D. External pressure**
	Performance Measurement Pressure: kwaliteit- en benchmarking van het Erasmus MC zijn de drijfveer voor de implementatie van de EEG caps (deductief) + Door de speerpunten van het Erasmus MC wordt ver digitalisering van de IC gestimuleerd - Door de vereisten en richtlijnen binnen het Erasmus MC is er minder vrijheid in de implementatie van nieuwe technieken
	I. Local attitudes
	Local Attitudes: Sociaal-culturele waarden (bijv. gedeelde verantwoordelijkheid) en overtuigingen (bijv. overtuigingen over de waardigheid van medewerkers) binnen het Erasmus MC moedigen aan om de implementatie en/of de levering van de EEG caps te ondersteunen (deductief)
3. Inner setting	**F. Access to knowledge & information**
	Access to Knowledge & Information: training/richtlijnen zijn beschikbaar voor de implementatie van de innovatie (deductief) + Er zijn gedocumenteerde afspraken over de indicaties voor monitoring - De implementatie van nieuwe EEG caps vergt nieuwe scholing en training van personeel
	G. Culture
	Deliverer-Centeredness: Er zijn gedeelde normen en waarden over het waarborgen van de wensen van de medewerkers van de KNF (deductief) + Er wordt onderling gesproken over zaken als werkdruk bij de KNF - Communicatie tussen verschillende functies over wensen vindt niet plaats **Recipient-Centeredness**: Er zijn gedeelde normen en waarden over het waarborgen van de wensen van de medewerkers van de IC (deductief) + Er wordt onderling gesproken over zaken als werkdruk op de IC - Intensivisten hebben andere wensen dan verpleegkundigen **Judgement**: De mate waarin er dezelfde mening heerst over de indicaties voor neuromonitoring middels EEG op de IC (inductief) + aanvragende en uitvoerende (IC, neurologie, KNF) afdelingen hebben dezelfde inschatting en zien bij dezelfde indicaties de noodzaak van EEG monitoring - De IC wil een sepsis patient monitoren, terwijl de KNF daar geen indicatie voor ziet

H. Structural characteristics

Work infrastructure: De organisatie van taken en verantwoordelijkheden binnen en tussen de KNF staf, assistenten, laboranten en IC staf en verpleegkundigen en de algemene personeelsbezetting ondersteunen de implementatie (deductief)
+ Iedereen weet wat zijn/haar taak en die van de andere betrokken is en waar de grenzen liggen
- De artsen koppelen zaken omtrent het EEG vaak niet terug aan verpleegkundigen

Information Technology Infrastructure: De technologische systemen voor telecommunicatie, elektronische documentatie, gegevensopslag, beheer, rapportage en analyse ondersteunen de implementatie (deductief)
+ EEG registraties zijn direct online beschikbaar en te beoordelen, er is een mogelijkheid tot real-time telemonitoring
- Niet alle elektronische systemen voor een efficiënte workflow zijn compatibel (BrainRT is niet gekoppeld aan HiX)

Physical Infrastructure: Lay-out en configuratie van ruimte en andere tastbare materiële kenmerken ondersteunen de implementatie (deductief)
+ De IC is met uitstek geschikt voor technische apparatuur voor het monitoren van patiënten
- Door de overvloed aan signalen op IC kamers is een draadloze verbinding ruisgevoelig

Workload: de werkdruk/belasting die personeel ervaart en de ruimte die er ligt om meer tijd te besteden aan EEG monitoring op de IC (deductief)
+ De IC is met uitstek geschikt voor technische apparatuur voor het monitoren van patiënten
+ Er is ruimte om de huidige workflow uit te breiden
- KNF laboranten ervaren een hoge werkdruk door tekorten

I. Available resources

Physical space: Er is fysieke ruimte beschikbaar op de patiëntkamer op de IC om EEG caps en apparatuur kwijt te kunnen (deductief)
+ Elke IC patiënt heeft een eigen kamer met veel ruimte voor apparatuur
- Bij een patiënt met multi-orgaan falen zijn soms meerdere monitorings- en ondersteunende apparaten in gebruik, waardoor er amper meer om te patiënt heen gelopen kan worden

Personal space: Er is ruimte voor de EEG caps om aangebracht te worden op het hoofd van de patiënt (inductief)
+ EEG caps bestaan in het format dat deze makkelijk om andere attributen heen geplaatst kunnen worden
- Door beademingsapparatuur en centrale lijnen is een cap op het hoofd van de patiënt soms moeilijk te plaatsen

Equipment availability: de mate waarin onderdelen die nodig zijn voor EEG monitoring op de IC beschikbaar zijn (inductief)
+ altijd voldoende apparatuur beschikbaar
- De apparaten zijn niet altijd voldoende beschikbaar

J. Mission alignment

Mission alignment: De implementatie van nieuwe EEG monitoring is in overeenstemming met de speerpunten van de KNF/IC (deductief)
+ Op de IC wil men graag meer monitoren van de hersenfunctie
- De speerpunten van de KNF richten zich meer op het diagnosticeren van epilepsie en slaapstoornissen dan op langdurige EEG monitoring op de IC

K. Relative priority

Relative Priority: De implementatie van EEG op de IC heeft prioriteit ten opzichte van andere initiatieven die lopen (deductief)
+ Binnen de KNF is de implementatie van EEG op de IC een speerpunt en topprioriteit
- Op de IC zijn continu implementaties en er is geen duidelijke implementatie met prioriteit

	L. Compatability
	Compatibility: De EEG caps kunnen makkelijk ingebed worden en samenwerken met de huidige workflow, systemen en processen (deductief) + De nieuwe EEG caps kunnen op de huidige apparatuur aangesloten worden en gelinkt worden aan de gebruikte informatiesystemen - Wanneer er meer gemonitord gaat worden met nieuwe caps en deze moeten aangesloten worden op de huidige apparatuur, kan er een tekort ontstaan aan apparatuur
	M. Tension for change
	Tension for change: De huidige situatie is ontolereerbaar en verandering is noodzakelijk (deductief) + De werkdruk op de KNF laboranten is te hoog en het plakken van EEG elektrodes is te arbeidsintensief - De huidige workflow werkt voorspoedig
	O. Communications
	Communications: Er zijn formele en informele praktijken van hoge kwaliteit voor het delen van informatie binnen en over de grenzen van de KNF, neurologie en IC (deductief) + In HiX wordt de uitslag van het EEG teruggekoppeld en telefonisch doorgebeld - Directe terugkoppeling naar de IC vindt nauwelijks plaats **Collaboration**: Hoe de betrokken individu(en) met elkaar samenwerken (inductief) + Er wordt samen naar een doel toegewerkt - Taken worden opgelegd door een persoon
4. Individual characteristics	**P. Motivation**
	Motivation: De individu(en) is toegewijd om zijn/haar rol bij de nieuwe manier van EEG monitoring te vervullen (deductief) + De respondent is gemotiveerd om prioriteiten in werkzaamheden te verschuiven om de implementatie te laten slagen - De respondent is niet gemotiveerd om de workflow aan te passen of meer te gaan werken om de implementatie te laten slagen
	Q. Capability
	Capability: De individu(en) heeft de kennis, skills en competenties om zijn/haar rol te vervullen (deductief) + De betrokken werknemers zijn goed geschoold en kunnen makkelijk schakelen naar nieuwe EEG caps - De betrokken werknemers (verpleegkundigen, intensivisten) hebben nog geen ervaring met EEG monitoring en moeten eerst bijgeschoold worden
	R. Need
	Need: De individu(en) heeft moeite met welzijn en/of persoonlijke voldoening, die zullen worden aangepakt door de implementatie (deductief) + De respondent heeft baat bij de implementatie omdat daardoor wetenschappelijk onderzoek uitgebreid kan worden - De betrokken persoon heeft zelf geen directe connectie met EEG monitoring en helpt degene niet verder in het dagelijks leven
	T. Trust
	Trust: De individu(en) heeft vertrouwen in de capaciteiten van het EEG en de analysemethodes + De arts ziet de toegevoegde waarde van het EEG en snapt wat het monitort - Automatische analyse van het EEG wordt niet vertrouwd totdat de arts zelf snapt wat het algoritme doet

C Questionnaire EEG technicians

Questionnaires were conducted in the Dutch language.

Algemeen

Tijdens dit onderzoek worden de huidige workflow, de knelpunten en den wensen omtrent neuromonitoring middels EEG op de volwassen Intensive Care van het Erasmus MC in kaart gebracht. Daarnaast wordt onderzocht wat de potentiële belemmerende en bevorderende factoren zijn voor de implementatie van nieuwe EEG apparatuur op de volwassen IC. In deze vragenlijst wordt u gevraagd om uw mening te geven over een aantal stellingen over EEG monitoring op de IC.

- Hoe lang bent u werkzaam in uw huidige functie als laborant binnen de KNF van het Erasmus MC (in jaren)?

Stellingen

Er volgen nu een aantal stellingen waarbij u kunt aangeven in welke mate u het (on)eens bent met de stelling. 1: helemaal oneens, 2: oneens, 3: neutraal, 4: eens, 5: helemaal eens.

- Ik vind dat ik genoeg tijd heb voor de werkzaamheden die komen kijken bij EEG monitoring op de volwassen IC.
- Ik ben op de hoogte van de indicaties voor EEG monitoring op de IC volwassenen.
- Ik heb plezier in de werkzaamheden die komen kijken bij EEG monitoring op de IC volwassenen.
- Ik denk dat er in de huidige logistiek ruimte is om meer te monitoren middels EEG op de IC.
- Ik ervaar een hoge werkdruk als laborant.
- Ik denk dat er bij bepaalde indicaties (zoals bij post-anoxie) ook met een ander systeem (zoals een cap in plaats van losse elektrodes) gemonitord zou kunnen worden.
- Ik denk dat het toegevoegde waarde kan hebben om meer IC patiënten te gaan monitoren middels EEG.
- Ik ben geïnteresseerd in wat extra EEG monitoring op de IC ons voor nieuwe inzichten kan geven.

Werkzaamheden

- Waar besteedt u als laborant het meeste tijd aan (1 = meeste tijd, 9 = minste tijd)
- Waar zou u het liefst het meeste tijd aan besteden? (1 = meeste tijd, 9 = minste tijd)
  - Poliklinische werkzaamheden praktisch
  - Klinische werkzaamheden praktisch
  - Poliklinische werkzaamheden (SPOED)
  - Klinische werkzaamheden (SPOED)
  - Beoordelen van EEG registraties
  - Administratieve werkzaamheden
  - Overleg
  - Onderwijs
  - IONM

U wordt gevraagd om een spoed EEG op de IC aan te brengen.

- Welke werkzaamheden kosten u het meeste tijd (1 = meeste tijd, 7 = minste tijd)

- Aan welke werkzaamheden zou u graag het meeste tijd besteden? (1 = meeste tijd, 7 = minste tijd)
  - Overleggen
  - Benodigde apparatuur verzamelen
  - Communiceren op/met de IC
  - Aanbrengen van de EEG elektrodes
  - Alles juist aansluiten
  - Opruimen
  - Wachten

Afsluiting

- Heeft u aanvullende suggesties om de huidige workflow rondom EEG monitoring op de IC volwassenen te verbeteren die nog niet in het interview besproken zijn?
- Wilt u na het interview en het invullen van deze vragenlijst nog iets kwijt?

Bedankt voor uw deelname!

D Questionnaire responses

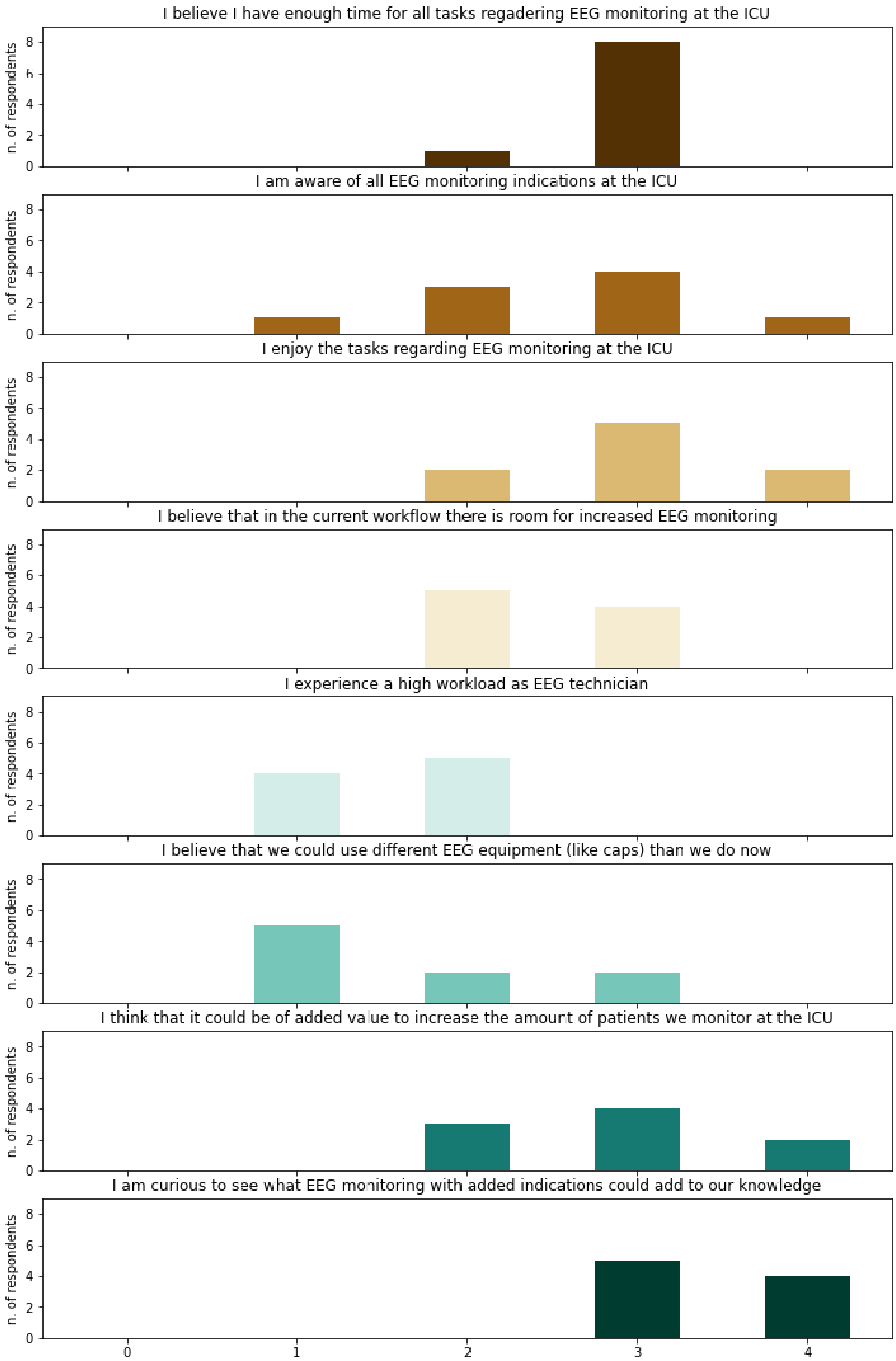


Figure D.1: Distribution of responses to the quotes in the questionnaire of electroencephalography (EEG) technicians (n=9). ICU: Intensive Care Unit. 0: fully disagree, 1: disagree, 2: neutral, 3: agree, 4: fully agree.

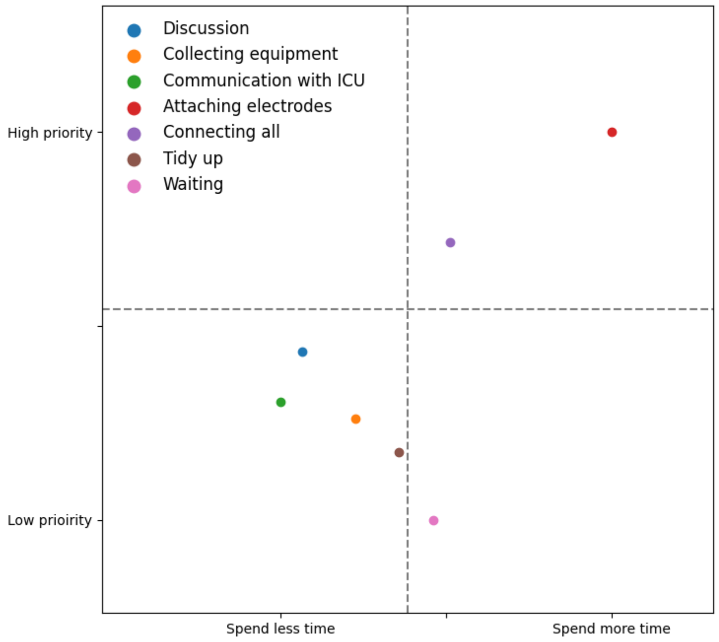


Figure D.2: Quadrant plot of usage of time versus priorities of tasks of electroencephalography (EEG) technicians (n=9) regarding EEG monitoring at the Intensive Care Unit (ICU). y-axis: the priority EEG technicians want to give to specific tasks. x-axis: the time EEG technicians usually spend on specific tasks.

E Suggestions

In this supplementary material, all suggestions provided during the interviews are summarised. Table E.3, E.4, and E.5 summarise all the suggestions made with regard to logistics, equipment requirements, and research opportunities.

Table E.3: Logistic wishes regarding electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital. EEG: electroencephalography. ICU: Intensive Care Unit. CN: clinical neurophysiology. PA: Physician Assistant. LEM: Long EEG Monitoring. OHCA: Out-of-Hospital Cardiac Arrest.

Subject	Suggestions
EEG attachment	Training ICU nurses to attach EEG caps for specific indications Develop a decision tree on which indications have the highest priority Only during regular working hours for new indications in a research setting (in case of attachment by EEG technicians) To appoint a neural practitioner or technical physician to daily checkup on the EEG electrode placement, detachment, etc. during implementation phase
Planning	Create room within current planning by adding a technician responsible for EEG at the ICU Assessment of several CN exams can be performed by the PA instead of resident, to increase EEG monitoring possibilities
ICU	Create dashboard with alarm to inform physicians when to contact the neurologist and/or clinical neurophysiologist Replace wake-up calls with EEG monitoring Neural practitioners as contact person at the ICU, connecting factor between ICU and neurology
Assessment	Create AI algorithm to detect all continuous normal EEG patterns, residents and staff can assess the remaining parts Do not perform continuous monitoring (LEM) in post-OHCA patients, but rather at 24 hours after OHCA. Developing strict protocols on which indications should and should not be monitored during the night.

Table E.4: Electroencephalography (EEG) equipment suggestions and requirements regarding EEG monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital. AI: Artificial Intelligence.

Subject	Suggestions & concerns
Hardware	Take into consideration the ICU environment: what kind of signals and noise are already present? Define different ICU scenarios and test the equipment accordingly Are the current hardware systems necessary or is it possible to communicate through Bluetooth? Integration of button to indicate patient care by ICU nurses possible to automatically mark as artefact?
Software	There should be a way to automatically alarm when the EEG needs to be assessed in case of extra monitoring In case of AI, it should be possible manually view at least a few pages of EEG recording A EEG viewing station in case of extra monitoring
Applicability general	The system should be easy to clean It should be possible to place electrodes close and tight to the scalp It should be possible to attacht the electrodes or cap without disturbing central catheters, breathing tubes, etc. Using stickers instead of glue The equipment should be applicable/adaptable to patients with decompressive craniectomy
Applicability ICU nurses	The electrode placement should go automatically, i.e. no measurement per electrode The electrodes and hardware should be easy to connect The systems should have a check: is everything well connected?

Table E.5: Suggestions & Research possibilities (n. of respondents = 10) for a more effective monitoring strategy. Respondents were asked to describe any interests and/or concerns for future research. EEG: electroencephalography. ICU: Intensive Care Unit. AI: Artificial Intelligence. OHCA: Out-of-Hospital Cardiac Arrest. TBI: Traumatic Brain Injury. RCT: Randomised Controlled Trial. NCSE: Non-Convulsive Status Epilepticus.

Subject	Suggestions
Monitoring	Monitoring all ICU patients to evaluate whether treating epileptic EEG features would improve outcome. Monitoring all ICU patients to quantify the percentage of patients with epileptic EEG features
Artificial Intelligence	Automatic classification of EEG background pattern Outcome prediction using AI Using AI to define EEG features correlated to the clinical status of the patient Using AI to detect changes in EEG recordings over time (asymmetry, amplitude, frequencies) Beware of overfitting based on an imbalance in input from EEG data compared to the clinical parameters
At the bedside	Providing one simple measure as an indicator and/or alarm
Study type	Retrospective analysis of OHCA, TBI data RCT: treat patients with evident NCSE, do not treat in case of evidence of no abnormal EEG activity, randomise treatment for the group in between RCT: EEG caps without wake-up-call versus wake-up-call Start with patients where a good neurological scoring is performed, to be able couple the EEG to outcome or a clinical parameter
Confounders	Correction in statistical models based on medication used, treatment plans, age, days at the ICU
Law	To clarify whether EEG recordings should always be visually analysed in real-time in case of research To clarify whether EEG recordings should always be visually analysed in case of clinical practice, or whether selecting several epochs would be allowed as well

F Barriers & Facilitators

In this supplementary material, all of the mentioned potential facilitators and barriers for the implementation of a new EEG monitoring workflow at the ICU of the Erasmus MC are summarised per domain of the CFIR (Innovation Characteristics (Table F.6), Inner Setting (Table F.7 and F.8), Outer Setting (Table F.9) & Individual Characteristics (Table F.10)).

Table F.6: Barriers & facilitators regarding changes for electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital in the CFIR domain: Innovation Characteristics. n. Number of times statements were mentioned. OHCA: Out-of-Hospital Cardiac Arrest.

Facilitators	n.	Barriers	n.
Clinical Practice			
The EEG could influence clinical decision making	2	For most indications, the impact on clinical practice is not known yet	14
The EEG is used to guide clinical management for some indications (like post-OHCA)	2		
In neurological/neurosurgical patients, a neurological examination is performed and can be coupled to EEG	1		
Practical complexity			
The EEG does not bother ICU nurses	2	The signal quality of EEG caps decreases over time	3
EEG caps would reduce the complexity of the attachment	2	A lot of steps are required to ensure a good signal quality	2
		EEG caps move quite easily	2
		EEG caps are harder to attach in case of thick hair	1
		EEG caps cannot be used in patients with an ICP catheter	1
		The configuration of wires etc. can be uncomfortable for the patient	1
		The attachment of EEG electrodes for good signal quality is challenging	1
Complexity			
Due to the complex nature of the EEG, it has high potential in detecting relevant brain activity	1	The interpretation of the EEG is very complex	6
EEG caps and/or less electrodes can be attached by anyone	1	The EEG is prone to artefacts	6
		The EEG is often misinterpreted by non-trained employees	3
		Thresholds for “normal” EEG activity are hard to define	1
		EEG analysis (features) are prone to confounders	1
Relative advantage			
In potential, the EEG can be used to detect deterioration of brain functioning early on and influence clinical management	4	Detection of bleeding, epilepsy or strokes often will not change clinical management	2
The EEG is able to reflect brain activity that we cannot see from the outside of the patient	2	The EEG often identifies biomarkers that are caused by confounders	2
The EEG could potentially reduce the amount of CT/MRI scans	1	Extra monitoring will only lead to a few % detection of cases	1
Triability			
Signal quality can be easily tested on healthy volunteers	2	The EEG has to be visually analysed when it is recorded (law?)	2
The EEG can be used in a research setting without having to visually analyse all signals	2		

Table F.7: Barriers & facilitators regarding changes for electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital in the CFIR domain: Inner Setting I. n. Number of times statements were mentioned. OHCA: Out-of-Hospital Cardiac Arrest. CN: clinical neurophysiology.

Facilitators	n.	Barriers	n.
Access to knowledge & information			
The EEG is included in protocols on the clinical management of some indications	2	At the ICU, there are no protocols and/or way to access information on EEG monitoring	3
EEG equipment availability			
For some indications, it is possible to pause the EEG recording to use the hardware for another patient before returning to the original patient	1	Hardware is not always available at the time of desired EEG monitoring	4
Personal space			
		EEG caps might be hard to attach on a patient with a breathing tube, central catheters, etc.	1
Physical space			
ICU patient rooms are designed to store a lot of technical equipment	2	There is a lot of signal noise present in ICU rooms	1
Collaboration			
Clinical neurophysiologists, residents and EEG technicians often communicate and efficiently work together	2	There is no direct collaboration between the ICU and the clinical neurophysiology	3
Since the OHCA protocol, ICU nurses are familiar with EEG technicians	1	Collaboration between the departments often is not efficient	3
Communication			
Monitoring guided guided clinical management is frequently discussed at the ICU, making direct feedback possible	1	Nurses often are not ready when the EEG technician appears, due to a lack in communication	2
Communication between EEG technicians and nurses is often satisfactory	1	Physicians often interpret someone else’s words inaccurately	1
		The ICU staff sometimes forgets to consult the clinical neurophysiologist in case of postanoxia	1
Compatibility			
There are many simple EEG systems available, specifically developed for ICU use	1	Not all EEG caps/electrodes are compatible with the current hardware	1
Deliverer-Centeredness			
Clinical neurophysiologists pay attention to the workload of EEG technicians	3		
Judgement			
There are protocols for certain indications, making judgement of indiciations easier	2	EEG is often requested without a relevant indication (according to clinical neurophysiology)	10
Mission alignment			
EEG monitoring at the ICU is one of the priorities/spearheads of the CN department	1		

Table F.8: Barriers & facilitators regarding changes for electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital in the CFIR domain: Inner Setting II. n. Number of times statements were mentioned. OHCA: Out-of-Hospital Cardiac Arrest. CN: clinical neurophysiology.

Facilitators	n.	Barriers	n.
Relative priority			
EEG monitoring at the ICU is a priority within the clinical neurophysiology department	1	ICU EEG monitoring might not give significant overall health benefit	1
Work infrastructure			
The current infrastructure allows for precise triaging	2	There is a shortage in EEG technician availability	3
There is room for urgency within the planning of EEG technicians, and planning can be easily adapted	2	If an EEG technician or resident has to work for 2 hours during the night, they cannot work the following day	
The clinical neurophysiology has an on-call service and often prioritises ICU EEG monitoring	1	Increased monitoring and application by ICU nurses asks for availability of equipment at the ICU, which is not possible in the current workflow	2
		There are no strict rules for when to or when not to perform EEG recording	1
		The current workflow is not efficient and therefore equipment is often not available for patient B, when patient A does not need the monitoring any longer or EEG technicians cannot attach the electrodes within working hours	1
		It is not possible to increase the amount of EEG recordings that should be visually assessed significantly	1
The EEG is often requested on time	1	There is a lack of equipment	1
Workload			
The workload of clinical neurophysiologists and residents is okay	5	There is no room for increased EEG electrode attachment by EEG technicians within the current workflow	6
EEG assessment of post-anoxia patients does not have high workload	1	There is no room for continuous visual assessment of EEG recordings	3
There is room for an increased amount of EEG electrode attachment at the ICU by EEG technicians	1	ICU nurses experience a high workload	2
LEM (cEEG) monitoring has lower workload than standard EEG monitoring for EEG technicians	1	Clinical neurophysiologists and residents often have on-call service	2
EEG monitoring could potentially lead to a decreased workload for ICU nurses (less wake-up calls)	1	Monitoring deterioration of brain functioning asks for a significant increase in EEG assessment	2
		Attachment of EEG electrodes has a high workload (hours, physical)	2
Physical infrastructure			
		Almost all post-anoxia monitoring happens at IC6, while the motivated neural practitioners work at IC4	1
Tension for change			
At the ICU, they miss the opportunity to monitoring the functioning of the brain in real time	2		

Table F.9: Barriers & facilitators regarding changes for electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital in the CFIR domain: Outer Setting. n. Number of times statements were mentioned.

Facilitators	n.	Barriers	n.
Local Attitudes			
		The costs of hospital care are not allowed to increase	2
		In general, change is difficult in every hospital	1

Table F.10: Barriers & facilitators regarding changes for electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) discussed during 12- individual and 2 focus group interviews with respondents from different departments within and outside of the hospital in the CFIR domain: Individual Characteristics. n. Number of times statements were mentioned. OHCA: Out-of-Hospital Cardiac Arrest. CN: clinical neurophysiology.

Facilitators	n.	Barriers	n.
Capability			
EEG technicians have expertise in high quality EEG electrode attachment	6	ICU nurses and staff do not have experience with the interpretation of EEG signals and often misinterpret the signals	5
Neural practitioners are specialised ICU nurses with loads of neurology knowledge	4	ICU nurses are not capable to attach EEG electrodes in a full montage (without at least 1 year of training)	1
There are four certified clinical neurophysiologists with ICU experience that work at the neurology department	4	ICU physicians are not familiar with the brain as a vital organ	1
The ICU is a technical space and nurses and physicians are used to new equipment being implemented	3		
At ICU4, there are many nurses that used to work at the neurological ICU	1		
Motivation			
Many ICU nurses are interested in neuro-patients (used to work at the neurological ICU)	4	A potential initial increase in workload and change in current workflow scares most employees	2
Clinical neurophysiology staff and residents are interested in the potential benefit of EEG monitoring at the ICU	2	Without clear benefit and direct influence on clinical decision making, motivation of some employees is lacking	2
Neural practitioners are excited to work with new neuromonitoring equipment and teach colleagues	2	Some ICU nurses think the EEG is too complex and are not motivated to put work into the implementation	2
EEG technicians enjoy EEG electrode attachment	1	Some employees do not like research, since they find that there often is no feedback on results of the study	2
		Not all clinical neurophysiologist are motivated to put extra work into ICU EEG monitoring	1
Need			
There is no way to evaluate the functioning of the brain in real-time	2	EEG technicians have no trouble with the time it takes to attach EEG electrodes	2
Trust			
Clinical neurophysiologists, residents and ICU staff see and trust the potential of ICU EEG monitoring	4	Clinical neurophysiologists and residents wonder what the potential benefit of ICU EEG monitoring will be	4
Clinical neurophysiologists and residents have a lot of trust in the capability of EEG technicians	3	People are sceptical/careful in their nature	3
EEG technicians and staff are able to quickly adapt to new EEG equipment and trust it	2	It can take up to a few years to gain every physicians trust at the ICU	2
Employees see increased continuous EEG monitoring at the ICU as the future	2	EEG technicians do not think EEG caps will work in the ICU environment	2
Employees trust that AI can significantly increase the value of EEG measurements	1	There is doubt in the added value of the standardised monitoring of OHCA patients at the ICU	2

G Implementation phase

Based on the identified barriers and facilitators for an effective implementation in a qualitative study on electroencephalography (EEG) monitoring at the Intensive Care Unit (ICU) of the Erasmus Medical Center Rotterdam (EMC), we identified the most important factors for the following implementation phase. Different scenarios for the reduction of workload and implementation of a new EEG worfklow at the ICU based on these factors, are discussed below.

- With a focus on reducing the current workload first, to be able to increase the effectiveness of future EEG monitoring
  - It is important to closely consider the preferences of various healthcare professionals, as this study has revealed discrepancies in the perspectives of different interviewees
  - Regular assessment and feedback sessions should be implemented to encourage all individuals involved and to address any challenges that arise
- Improving the interdepartmental collaboration
  - Assigning a key-figure that stays in contact with all involved employees and has the final responsibility for the implementation process and regular evaluations
  - Assigning a responsible persons per department involved to create an implementation team
- Deciding on the most promising indications for EEG monitoring
  - Emphasis should be layed on the effectiveness of EEG monitoring, i.e. the influence on clinical management and patient outcome
  - Do not only consider new indications, but pay attention to the effectiveness of EEG monitoring in the current indications
- Exploring how to deal with the different ICU sections (general versus cardio-thoracic)
- Deciding on who and how to train for the application of new EEG equipment

Workload

Reducing the workload of EEG technicians and ICU nurses should be a top priority. However, this should be tackled in different ways as the ICU nurses experience a high workload in so called wake-up calls, while the workload of EEG technicians has more to do with the EEG electrode attachment. Scenarios are described in Table G.11.

Interdepartmental collaboration

To ensure effective implementation, a key figure with final responsibility should be assigned (Table G.12). Additionally, a responsible representative per (sub)department should be appointed, to form an implementation team. These representatives could be:

- Clinical neurophysiology: keyfigure (Table G.12), additionally the two persons who end up not being the key figure
- ICU: neuro-intensivist and all three neural practitioners
- Neurosurgery: neurosurgeon with regular ICU supervision
- Neurology: neurologist with regular ICU supervision
- If possible: a neurology and neurosurgery resident

Approach for change

In Table G.13, some suggestions regarding the start of the implementation phase are provided.

Table G.11: Different scenarios and their (dis)advantages to reduce the workload of electroencephalography (EEG) technicians and Intensive Care Unit (ICU) nurses.

Scenario	Advantages	Disadvantages
Reducing the workload of EEG technicians by implementing new EEG equipment, facilitating easier attachment of electrodes	Quick EEG technicians have a lot of knowledge Creating space for monitoring of new indications, possibly leading to reduced amount of wake-up calls	EEG technicians are skeptical about other equipment In the end, the workload for EEG technicians might not be reduced
Reducing the workload of EEG technicians by reducing the amount of electrodes that should be attached in certain indications, facilitating easier attachment of electrodes	Quick EEG technicians have a lot of knowledge Creating space for monitoring of new indications, possibly leading to reduced amount of wake-up calls	In the end, the workload for EEG technicians might not be reduced
Reducing the workload of EEG technicians by teaching ICU nurses how to apply EEG caps	Quick ICU nurses are generally motivated Neural practitioners can be super-users	Implementation may take a longer time Exact localisation of electrodes may be limited Signal quality may be reduced

Table G.12: Possiblities of a responsible key figure to improve interdepartmental collaboration and the (dis)advantages. EEG: electroencephalography. ICU: Intensive Care Unit.

Scenario	Advantages	Disadvantages
Technical physician	Knowlegde of clinical and technical relevance Trained in interdisciplinary communication	Might lack knowledge on EEG equipment Not embedded in current workflow
Physician assistant	Knowledge of clinical and technical relevance Experience with EEG equipment and assessment	Lot of other responsibilities Does not have time to visit ICU on a daily basis
Clinical neurophysiologist	Knowledge of clinical and technical relevance High in hierarchy, personally knows most people involved	Lot of other responsibilities Does not have time to visit ICU on a daily basis

Table G.13: Options for the approach of change in the current workflow and their (dis)advantages. EEG: electroencephalography. ICU: Intensive Care Unit. CA: Cardiac Arrest.

Scenario	Advantages	Disadvantages
Using different equipment or amount of electrodes in the biggest group (postanoxic encephalopathy)	Potentially large effect possible to compare to the current standard	Most post-CA patients at cardiothoracic ICU, while neural practitioners only work at the general ICU
Introducing new EEG equipment for new research applications without altering the current workflow.	Reduction of workload of ICU nurses might be realised sooner Possible to focus on step by step implementation	Might not reduce workload of EEG technicians

H Description of dataset

All consecutive postanoxic comatose patients admitted to the ICU of the Erasmus MC, Rotterdam, between October 5th 2019 and April 25th 2023 were included in this study. continuous electroencephalography (cEEG) was part of standard clinical practice and used to guide neurological prognostication. Eventually, 327 patients with 38873 20-second EEG epochs were used for the analyses (Figure H.3). The distribution of different background patterns at 24 hours after Cardiac Arrest (CA) (the moment of neuroprognostication according to the national guidelines [1]) of the included patients in this study is visualised in Figure H.4. The most common background patterns at 24 hours after cardiac arrest (T24) were a continuous background pattern, Burst Suppression (BS) with non-identical bursts.

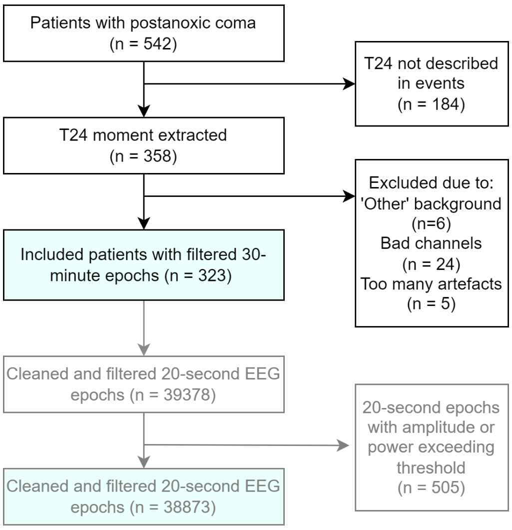


Figure H.3: Flowchart of patient- and epoch inclusion. Out of 542 electroencephalography (EEG) recordings at 24 hours after cardiac arrest, 323 were included in the study.

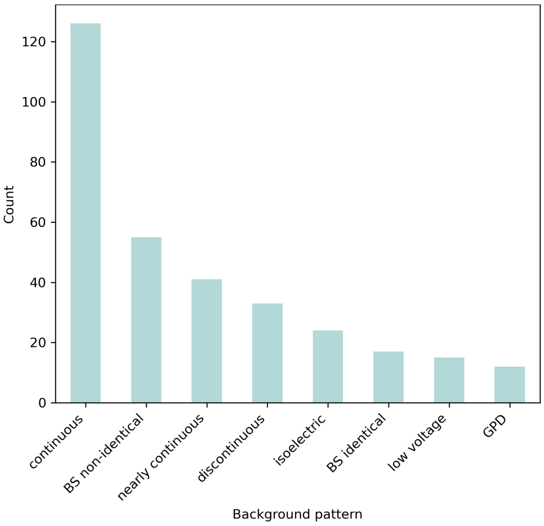


Figure H.4: The distribution of EEG background patterns at 24 hours after cardiac arrest in the included patients in this study (n=323) based on the visual assessment of the EEG. BS: Burst Suppression, GPD: Generalised Periodic Discharges.

I EEG background patterns

In this supplementary material, examples of the 8 different categories of EEG background patterns that were classified in this study are provided. 15 seconds of EEG background patterns surrounding the T24 moment are displayed in Figure I.5, I.6, I.7, I.8, I.9, I.10, I.11, and I.12.

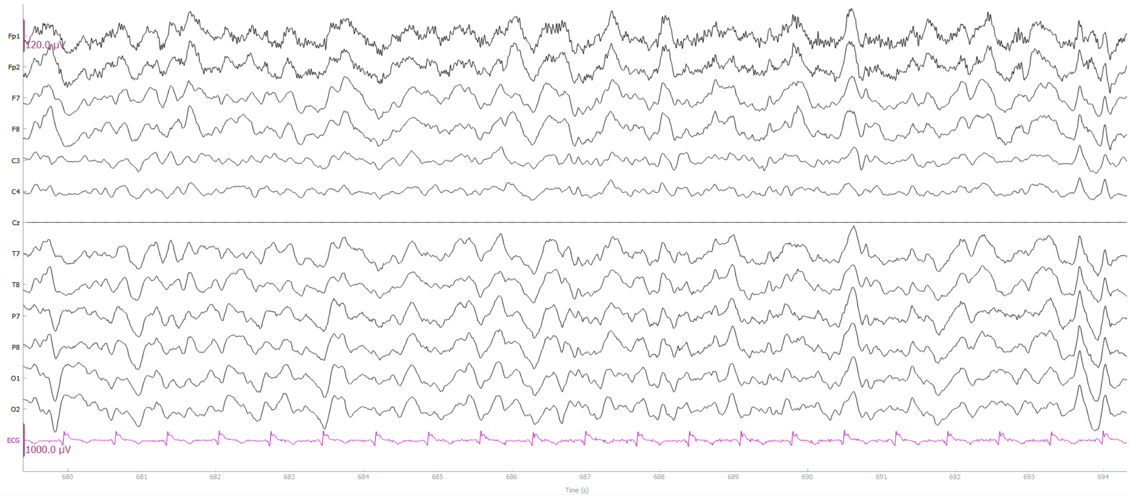


Figure I.5: Continuous background pattern. Cz-referenced, displayed at 120 μV, 15 seconds (sub-0118).

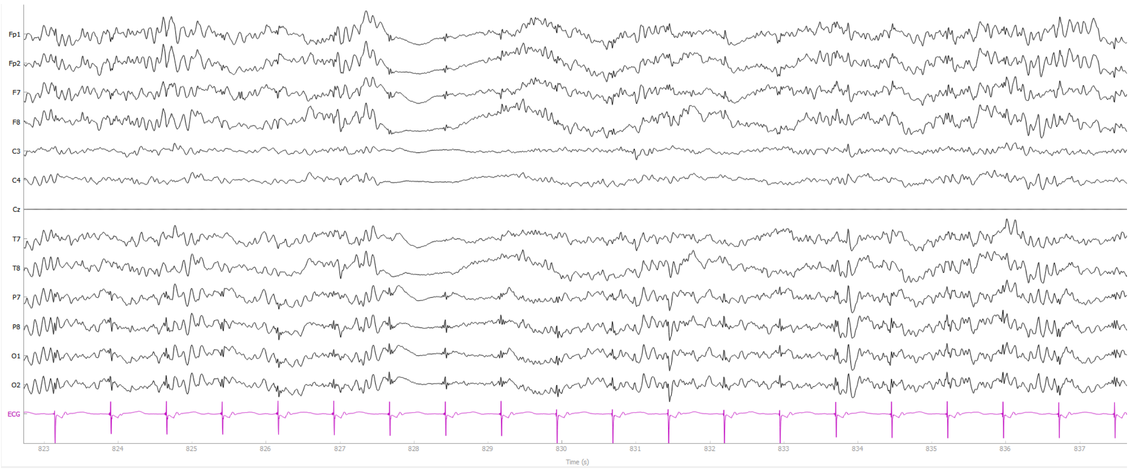


Figure I.6: Nearly continuous background pattern. Cz-referenced, displayed at 80 μV, 15 seconds (sub-0020).

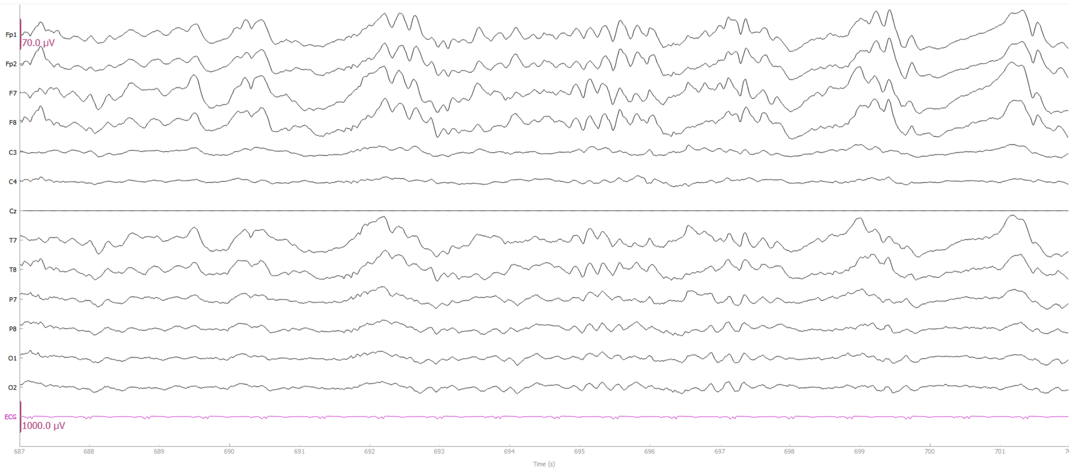


Figure I.7: Discontinuous background pattern. Cz-referenced, displayed at 70 μV, 15 seconds (sub-0074).

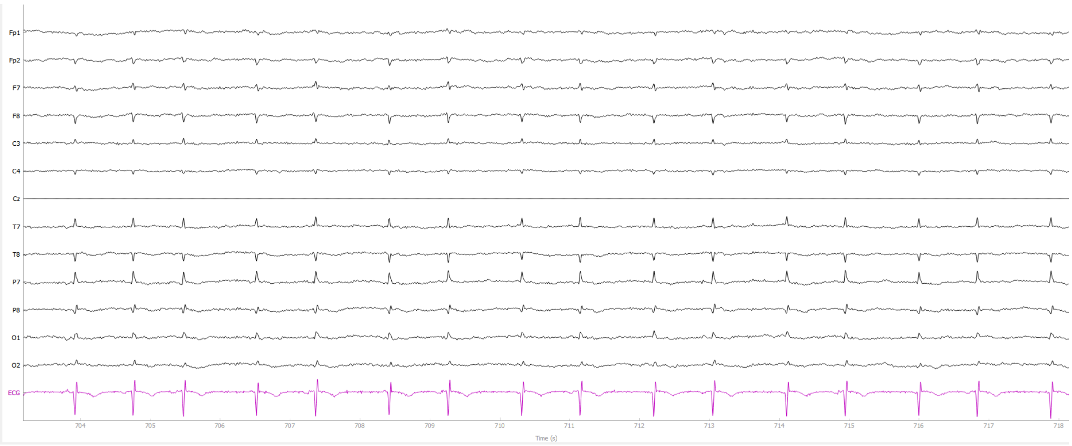


Figure I.8: Isoelectric background pattern. Cz-referenced, displayed at 10 μV, 15 seconds (sub-0015).

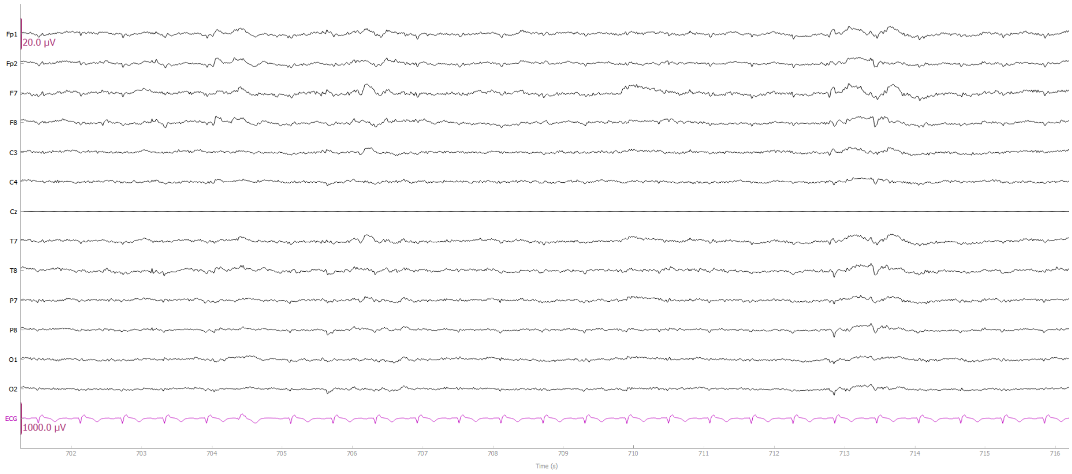


Figure I.9: Low voltage background pattern. Cz-referenced, displayed at 20 μV, 15 seconds (sub-0010).

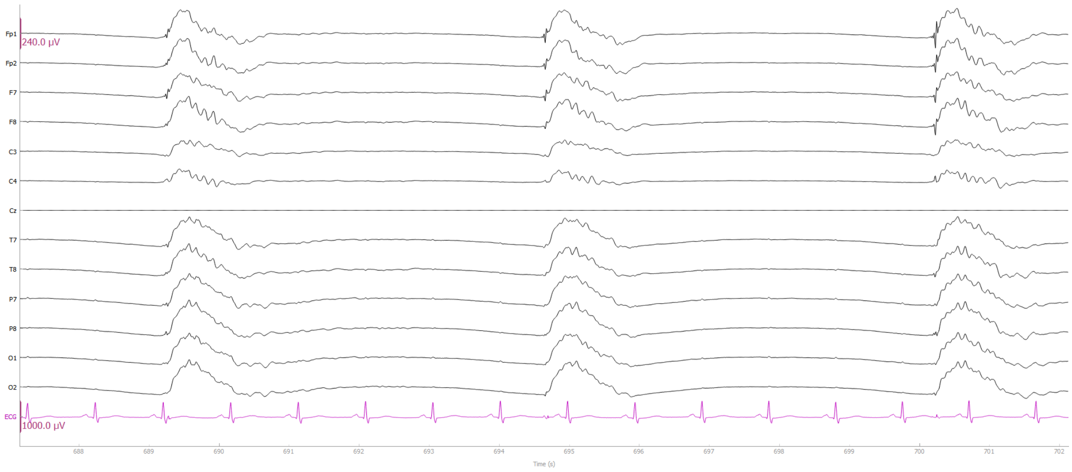


Figure I.10: Burst-suppression with identical bursts. Cz-referenced, displayed at 240 μV, 15 seconds (sub-0220).

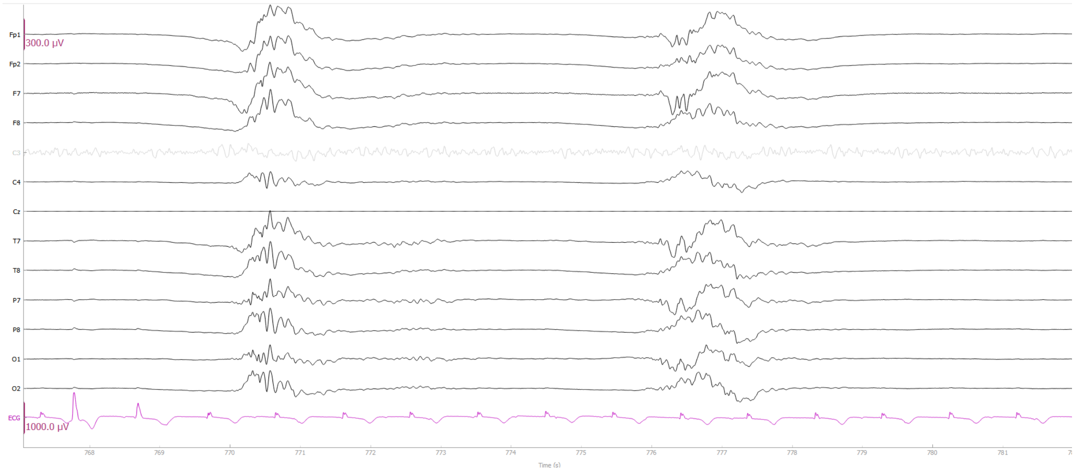


Figure I.11: Burst-suppression with non-identical bursts. Cz-referenced, displayed at 300 μV, 15 seconds (sub-0139).

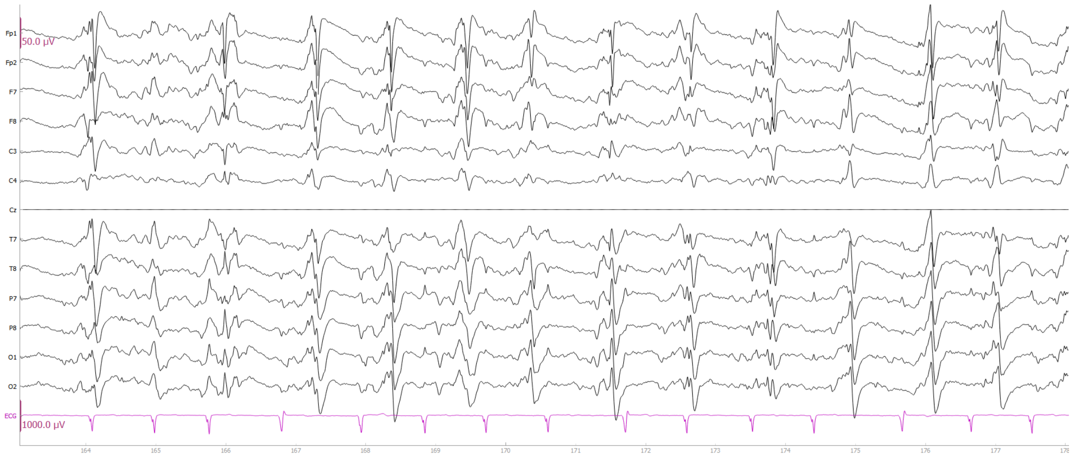


Figure I.12: Generalised Periodic Discharges. Cz-referenced, displayed at 50 μV, 15 seconds (sub-0303)

J Preprocessing

In this supplementary material, the preprocessing steps of the EEG data are further elaborated upon. All data was stored following the international Brain Imaging Data Structure for EEG (BIDS-EEG) structure to facilitate organisation and sharing possibilities of data. [2]

Bad channels and artefacts

30-minute epochs surrounding the T24 moment were visually inspected to identify loose EEG channels and major artefacts. Since it was assumed that there would be minimal artefacts in this patient population (partly due to patients being sedated and not moving), extensive artefact detection was not performed. Significant artefacts caused by activities such as patient care by nurses were manually removed from the data, but artefacts resulting from electrode pops, for example, were not thoroughly examined. Bad segments and loose channels were marked in the MNE toolbox and subsequently excluded from further analyses. Datasets with loose channels were excluded entirely from the analyses to ensure that the baseline group did not include any patients with fewer than 12 electrodes. This approach allowed for an unbiased evaluation of the effect of removing a specific number of electrodes. In addition to the visual inspection of artefacts, remaining artefactual epochs were removed based on amplitude and total Power Spectral Density (PSD). The amplitude of all 20-second epochs was calculated, and a threshold was set at 300 μV, as physiological brain activity will not exceed this voltage. Subsequently, the threshold for the total power was set at 2000 W/Hz. All epochs exceeding these threshold were removed from further analysis.

The presence of the ECG artefact, caused by the electrical activity of the heart, is a common issue in EEG recordings. To mitigate this artefact, a widely employed approach is performing Independent Component Analysis (ICA) analysis. In this study, the MNE toolbox's automatic ECG removal using ICA analysis (Reparing artefacts with ICA) was utilised. Using this method, the first 10 ICA components were selected. A threshold was set at 0.9 for the Pearson correlation value between the ICA component and the electrocardiogram (ECG) signal. Components above this threshold were removed from the data. However, it is important to note that complete removal of ECG artefacts was not achieved, which warrants attention in future studies.

Filtering

EEG signals are prone to noise and artefacts, which can distort the data and hinder the identification of meaningful patterns. Applying appropriate filters helps eliminate unwanted components and emphasise the underlying brain activity of interest. This preprocessing step enhances the quality of the EEG data, enabling more accurate quantitative analysis and interpretation. Filters can have significant effect on EEG analysis, especially in the case of Evoked Response Potentials (ERP). However, since this analysis primarily focused on the overall EEG background pattern and not the precise timing of specific patterns, it was determined that the default settings of the MNE filters would be sufficient. The default settings of the MNE notch-filter to remove power-line noise at 50 Hz were used. Additionally, a bandpass filter from 0.5 to 35 Hz was used. Both filters were designed as non-causal Finite Impulse Response (FIR), meaning that the data was first filtered forward and then again backward to limit the introduction of phase delays in the signal.

Notch filter

- Windowed time-domain design (firwin) method
- Hamming window with 0.0194 passband ripple and 53 dB stopband attenuation
- Lower passband edge: 49.38
- Lower transition bandwidth: 0.50 Hz (-6 dB cutoff frequency: 49.12 Hz)
- Upper passband edge: 50.62 Hz
- Upper transition bandwidth: 0.50 Hz (-6 dB cutoff frequency: 50.88 Hz)
- Filter length: 1691 samples (6.605 sec)

Bandpass filter

- Windowed time-domain design (firwin) method
- Hamming window with 0.0194 passband ripple and 53 dB stopband attenuation
- Lower passband edge: 0.50
- Lower transition bandwidth: 0.50 Hz (-6 dB cutoff frequency: 0.25 Hz)

- Upper passband edge: 35.00 Hz
- Upper transition bandwidth: 8.75 Hz (-6 dB cutoff frequency: 39.38 Hz)
- Filter length: 1691 samples (6.605 sec)

Rereferencing

Two commonly used rereferencing methods are average rereferencing or the use of a reference electrode that is physically distant from the scalp and has minimal cerebral activity, such as the mastoid or ear electrode. However, such an electrode is usually not attached in postanoxic ICU patients and could not be used in this retrospective study. Furthermore, average referencing, which is commonly used in quantitative EEG analysis, was deemed unsuitable due to the changing average with each new electrode configuration. Furthermore, an average reference based on only 4 electrodes might not be ben Since neutral electrodes were not utilised during EEG recording, it was decided to adopt Cz as a common reference for all analyses (Figure J.13). However, it is important to acknowledge that focal abnormalities at the Cz location could have influenced the study's outcomes. Moreover, amplitudes at the C3 and C4 electrodes would appear lower compared to more distant electrodes, as greater inter-electrode distances tend to increase signal amplitudes. Additionally, the choice of Cz reference could potentially impact several features. For instance, when calculating electrode coherence, if the activity measured at Cz dominates over other electrodes, the coherence measurement may mainly reflect the coherence between Cz activity and itself.

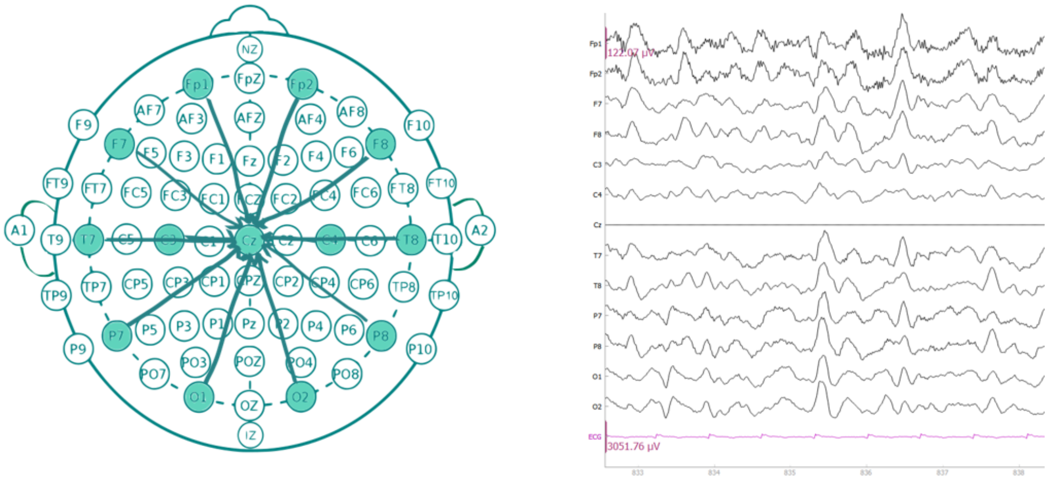


Figure J.13: Cz common reference used as rereferencing method in this study. The traces that are visualised represent the voltage differences between the electrical charge at that electrode and the Cz electrode.

Epoch length

To determine the optimal length of epochs for EEG feature calculation, the mean, minimal, and maximum amplitude distributions per epoch were compared across different lengths (Figure J.14). Epochs of 10, 20, and 30 seconds were created for this analysis. The comparison was based on EEG data from 10 patients (sub-0000 to sub-0010), of which 7 had usable data at T24. The analysis of the feature distributions revealed that the length of an epoch did not significantly impact the amplitude values. As expected, the computational time was influenced by the epoch length, with shorter epochs requiring less computation time. Considering that some EEG background patterns after cardiac arrest may persist for periods longer than 10 seconds (like a burst-suppression pattern that can have periods of suppression of more than 10 seconds), a decision was made to select epochs of 20 seconds for further analysis. After the decision of the epoch length was made, a comparable analysis was performed to determine the optimal length of overlap in the epochs (0, 5, and 10 seconds). This analysis revealed that the inclusion or exclusion of overlap in epochs has minimal impact on the majority of features, except for measures such as entropy (Figure J.15). The difference between 5 and 10 seconds of overlap is negligible, while a noticeable distinction exists between 0 and 5/10 seconds. Given the emphasis on capturing overall EEG characteristics and anticipating limited variability within the 30-minute epochs, opting for overlapping epochs was deemed to be the most suitable approach. To enhance computational efficiency, a 5-second overlap was selected, resulting in an epoch length of 20 seconds with 5 seconds of overlap.

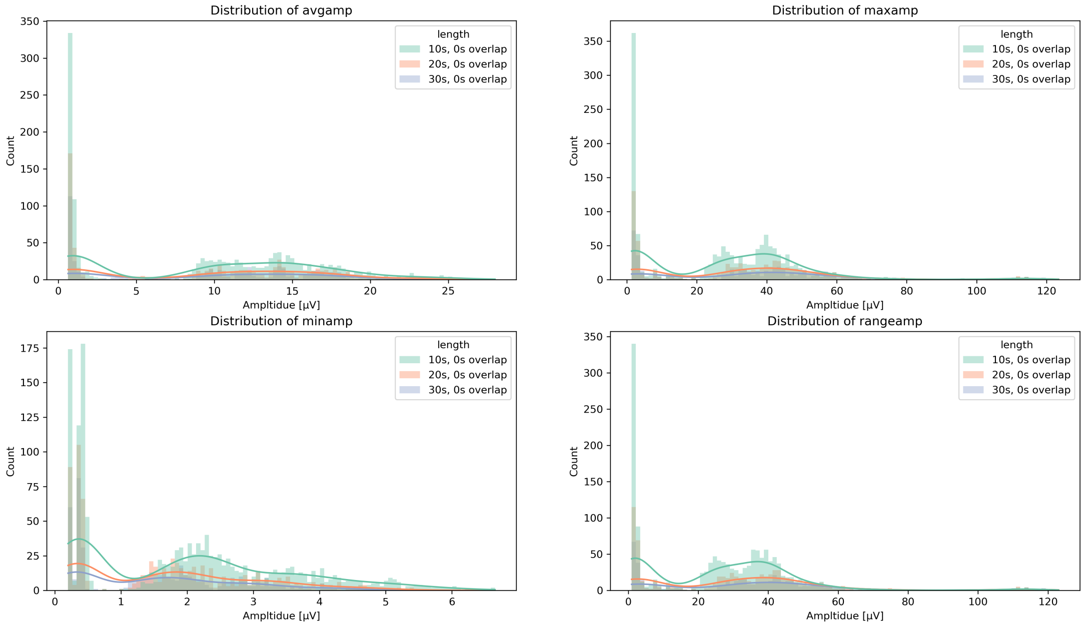


Figure J.14: Distribution of mean, maximum, minimum, and range of amplitudes in electroencephalograph (EEG) epochs of 10 versus 20 versus 30 seconds.

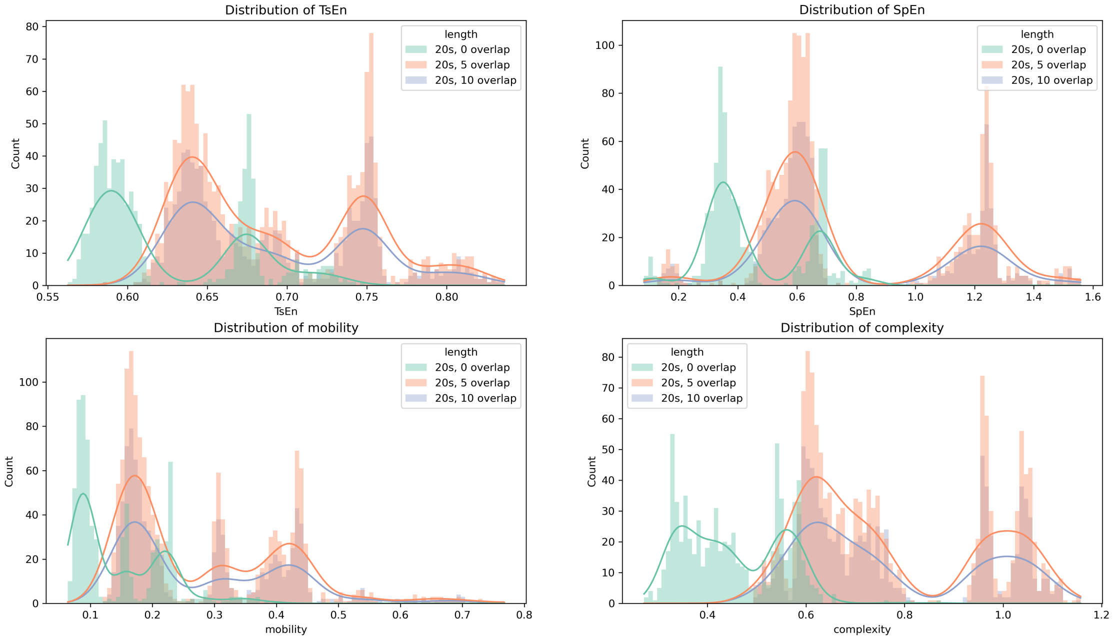


Figure J.15: Distribution of entropy and Hjorth features in electroencephalography (EEG) epochs of 20 seconds with 0 versus 5 versus 10 seconds of overlap. TsEn: Tsallis Entropy. SpEn: Spectral Entropy.

Description of preprocessing code

The source code for the preprocessing steps used in this study can be found at github and is visualised in Figure J.16.

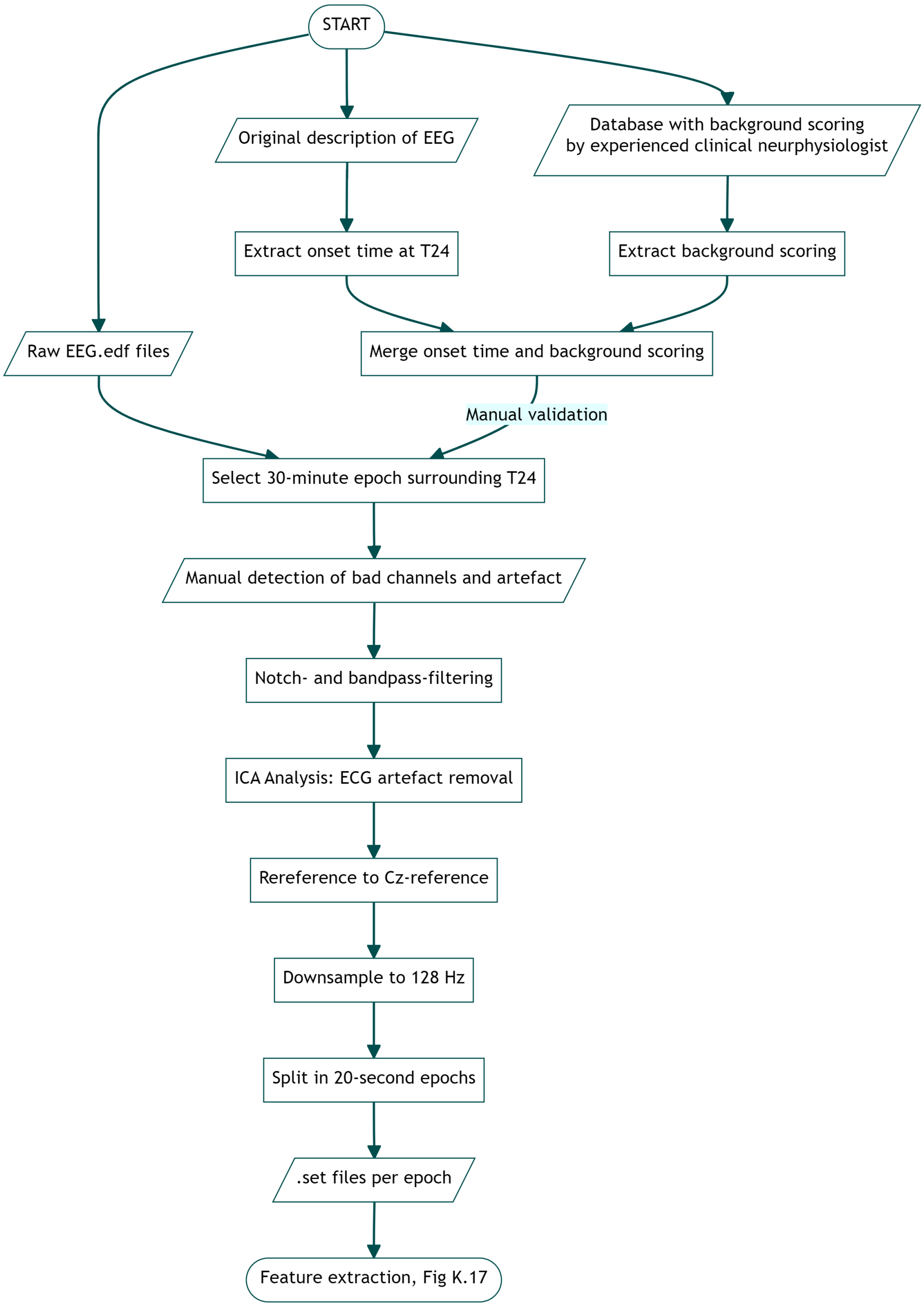


Figure J.16: Code flowchart of all steps that were taken in the electroencephalography (EEG) data preprocessing before EEG feature calculation.

K Features

In this supplementary material, a description of all included quantitative electroencephalography (qEEG) features is provided in alphabetical order. Feature calculation was performed in MATLAB, and the source code can be found through github. The workflow for the feature calculation is visualised in Figure K.17. For each included patient in this study, we calculated a total of 26 qEEG features. These features were first computed per epoch for each individual EEG channel. These channel values were then averaged to generate a single value per feature per epoch, which subsequently was averaged to result in a final feature value per patient.

Amplitude

The amplitude (in μV) of the EEG signal was calculated for every channel. A moving-average filter was applied to the absolute values of the EEG epoch. The moving-average filter had a window of 0.25 times the sample frequency. The average, minimum, maximum, and range of the amplitudes per epoch were calculated as features.

Bivariate Correlation Directed (BCorrD)

The Bivariate Correlation Directed (BCorrD) is a feature based on the Pearson correlation coefficient, [3] and first described by Wang et al. (2014). [4] The prefix B indicates bivariate methods using pair-wise calculations, and D indicated direct connectivity. Thus, BCorrD is a bivariate correlation method for measuring directed connectivity. The Pearson correlation coefficient has a value between -1 and 1 and reflects a linear correlation of variables. The BCorrD in this study was used to calculate the correlation between a channel, and a delayed version of itself using the Matlab function `xcov`.

Burst Suppression Ratio

The Burst Suppression Ratio (BSR) is defined as the percentage of time in which the EEG shows a suppression pattern, where high voltage burst activity alternates with periods of little or no activity (<5 μV). The BSR is calculated by dividing the total time that the EEG shows a suppression pattern by the total recording time.

$$BSR = \frac{T_{sup}}{T_{total}} \cdot 100\% \tag{1}$$

where:

T_{sup} : Duration of segments with amplitude $<$5 μV
T_{total} : Total duration of the EEG signal

The BSR varies between 0 and 1, where a BSR closer to 1 indicates a higher ratio of suppression of electrical brain activity.

Coherence

Coherence is an EEG feature that reflects the functional connectivity between different brain regions. It is a measure of the degree of synchrony between two EEG signals recorded from different scalp locations, and is thought to reflect the strength of the underlying neural connections. [5] In this study, the magnitude-squared coherence was calculated using the Matlab function `mscohere`. [6] The coherence value ranges from 0 to 1, with a value of 1 indicating perfect coherence, or complete synchronisation between the two EEG signals at frequency f, and a value of 0 indicating no coherence, or complete desynchronisation between the two EEG signals at frequency f.

EEG Silence Ratio (ESR)

The EEG Silence Ratio (ESR) is quite similar to the BSR and was calculated following the definition provided by Theilen et al. (2000). [7] The ESR is the fraction of total EEG length of which the EEG voltage remains below 5 μV for a duration of at least 240 milliseconds.

$$ESR = \frac{T_{sup}}{T_{total}} \cdot 100\% \tag{2}$$

where:

T_{sup} : Duration of segments with amplitude $<$5 μV for $>$240 ms
T_{total} : Total duration of the EEG signal

An ESR close to 0 indicates that there are (almost) no silent periods within the EEG, whereas a higher ESR value indicates more discontinuity.

Entropy

In this study, three different types of entropy were calculated.

Approximate Entropy

The Approximate Entropy (ApEn) is a measure of regularity that quantifies the unpredictability of fluctuations in a nonlinear time series, with a relatively higher value indicating a lower likelihood of similar patterns being followed by additional similar observations. [8] In the context of EEG, the ApEn calculates the predictability of future amplitude values in the EEG by considering the knowledge of the preceding amplitude values. The ApEn was calculated using the Matlab function `approximateEntropy`.

Tsallis Entropy

The Tsallis Entropy (TsEn) is an entropy measure that captures the complexity and regularity of a signal by analysing the different frequency components of the signal. [9] It not only takes into account the spectral properties of a signal, but introduces an additional parameter that results in non-extensive statistics (independent of initial conditions). The Tsallis Entropy was calculated using the `weentropy` function of Matlab.

Spectral Entropy

The Spectral Entropy (SpEn) is a measure of the uniformity of the spectral power distribution of a signal. [10] For a more uniform distribution, the spectral entropy is larger. In this study, the SpEn was calculated with the use of the `pentropy` function of Matlab In this function, the Shannon entropy of the normalised energy is calculated.

Hjorth parameters

Hjorth parameters are a set of three descriptors used to characterise the characteristics of a time series in the time- and frequency domain. [11] The activity represents the overall magnitude of the signal and is calculated by measuring the variance of the signal. Activity increases for a signal with higher frequencies. Mobility is a measure of the standard deviation of the power spectrum and complexity compares the similarity of the signal to a sine wave (a value of 1 means that the signal is more similar to a sine wave).

$$activity = var(y(t)) \tag{3}$$

$$mobility = \sqrt{\frac{var(y'(t))}{var(y(t))}} \tag{4}$$

$$complexity = \frac{mobility(y'(t))}{mobility(y(t))} \tag{5}$$

where:

$y(t)$: The time-series signal

Phase Lag Index

The Phase Lag Index (PLI) is a measure of functional connectivity and is used to calculate the asymmetry of the phase lags between two EEG channels by estimating the proportion of time in which the phase difference between them remains consistently in the positive or negative direction. [12] The PLI ranges from 0 to 1 and a higher PLI indicates stronger phase synchronisation between brain regions.

Power Spectrum

The power spectrum, the power in frequency components of the signal, was calculated using the Matlab function `bandpower`. This function calculates the power spectrum with a Fast Fourier Transform (FFT) with a Hamming window. Using this function, the absolute power per frequency band and the relative power (the fraction of the power in a specific frequency band compared to the total power) were calculated.

- total: 0.5 - 25 Hz
- delta: 0.5 - 4 Hz
- theta: 4 - 8 Hz
- alpha: 8 - 13 Hz
- beta: 13 - 25 Hz

Regularity

The regularity was first described by Tjepkema-Cloostermans et al. (2013) to evaluate the regularity of the amplitude of a signal. [13] The EEG signals were squared, and subsequently the values of the signal were sorted in descending order. Finally, the normalised standard deviation was calculated. A signal with low amplitudes and bursts has a regularity value close to zero, whereas signals with constant amplitudes have a value close to 1.

$$Reg = \sqrt{\frac{\sum_{i=1}^{N} i^2 q(i)}{\frac{1}{3} N^2 \sum_{i=1}^{N} q(i)}} \tag{6}$$

where:

N : length of the signal
q : sorted signal

Spectral Edge Frequency

The Spectral Edge Frequency (SEF) is defined as the frequency below which a specified percentage of the total power of the signal is contained. In this study, the SEF at 95% was calculated, which represents the frequency below which 95% of the total power of the signal is concentrated. The SEF at 95% is often calculated in EEG analysis, especially to assess the depth of sedation. [14]

Spikes

Epileptic spikes were defined as waves with a high amplitude and maximum duration of 70 milliseconds. In this study, spikes were calculated with a threshold for the amplitude of at least 2.5 times the standard deviation from the mean signal. [15]

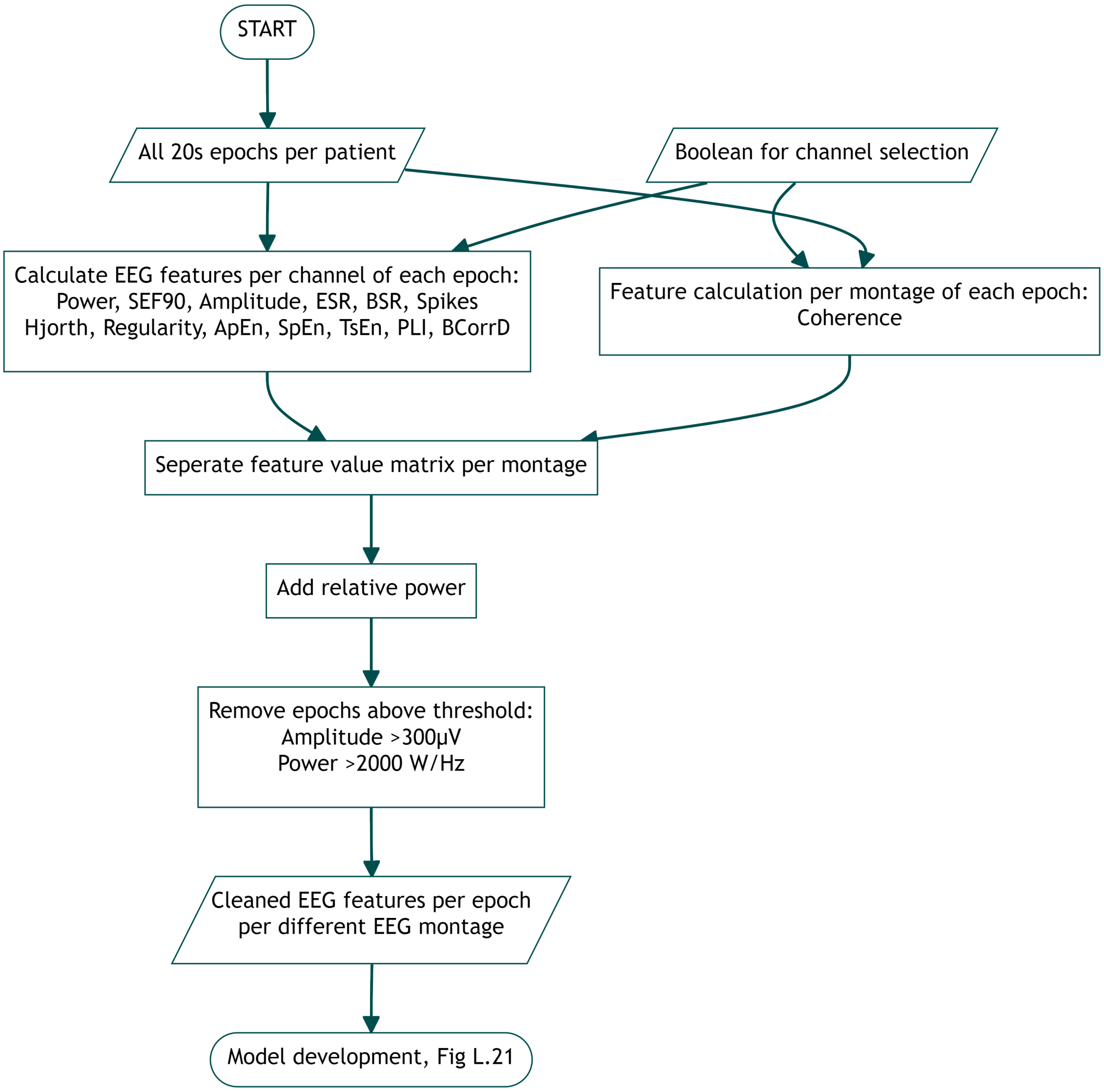


Figure K.17: Code flowchart of the electroencephalography (EEG) feature calculation in this study. For nearly all features, feature values per channel were calculate and based on the number of EEG electrodes used as input, the mean feature value was calculated. The coherence was separately calculated for each combination of electrodes included in this study.

Feature distribution per EEG background category

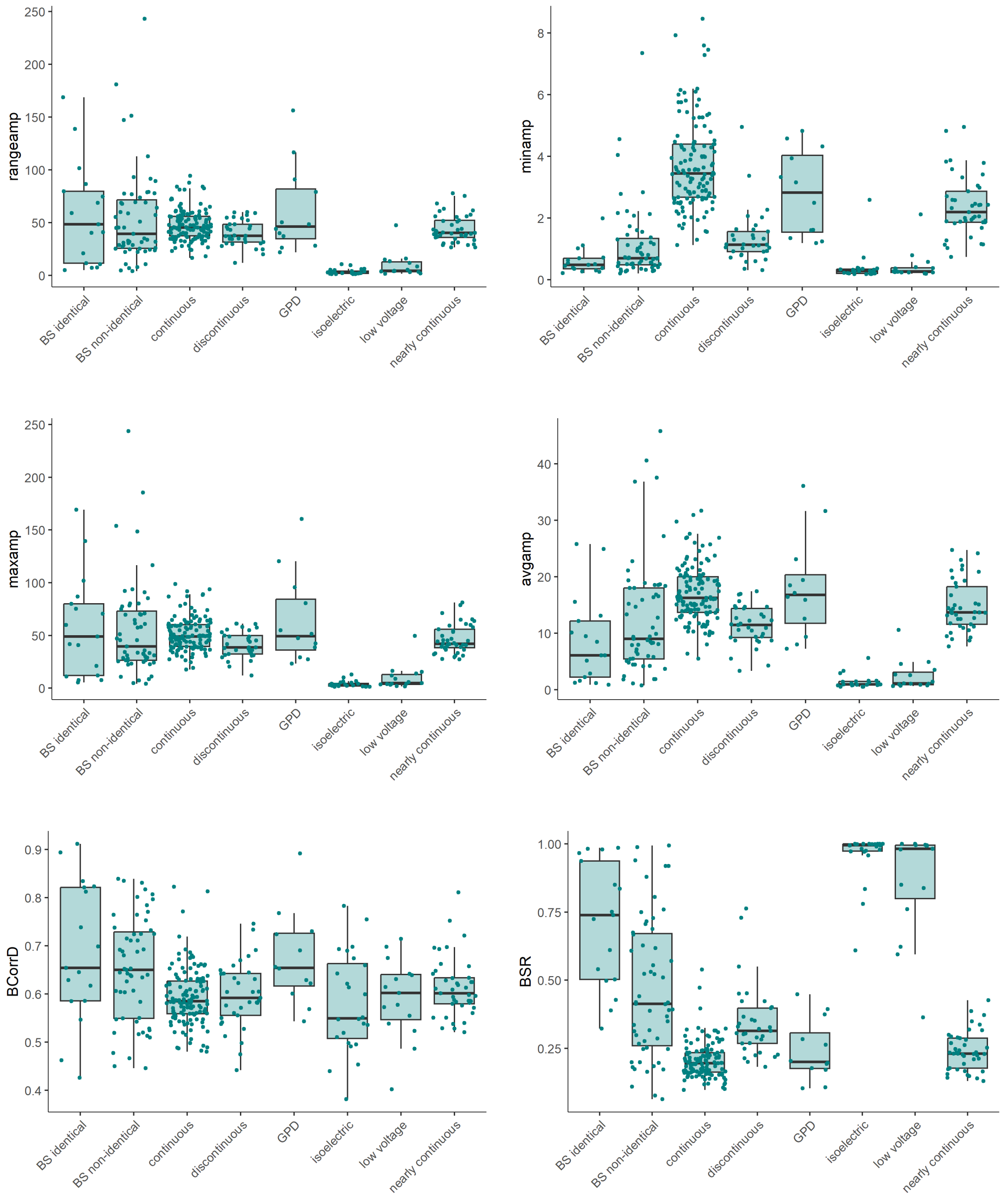
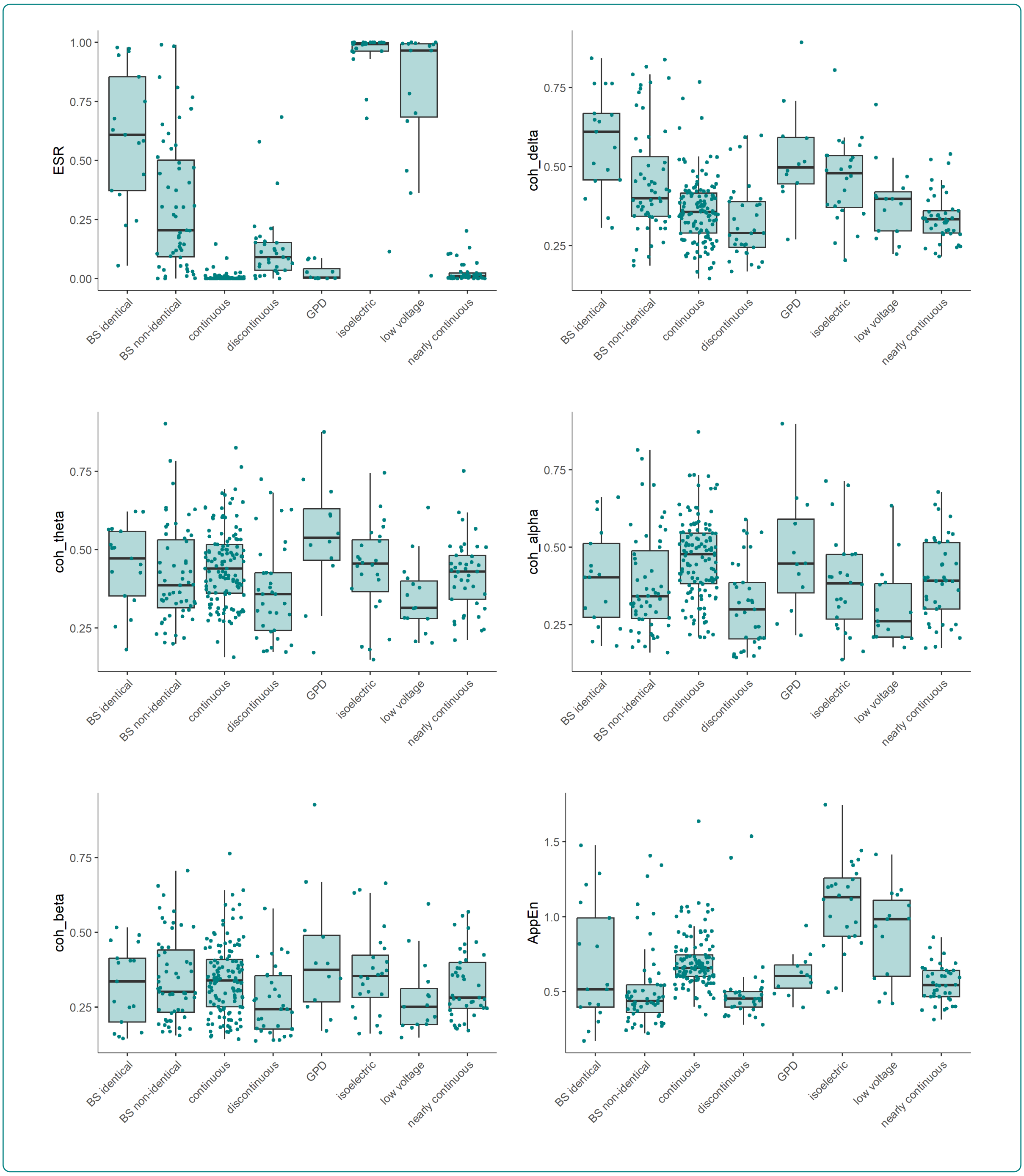
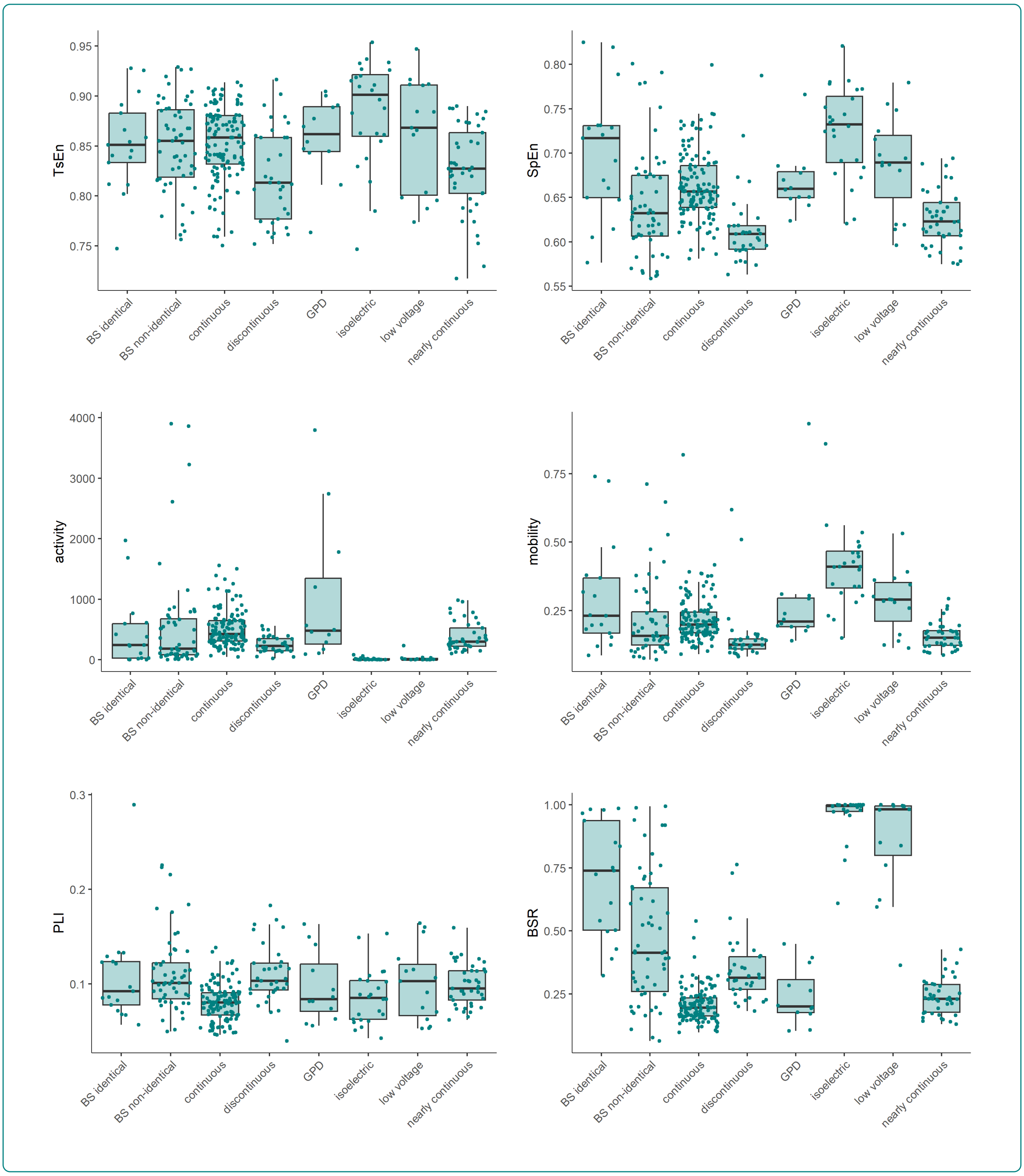
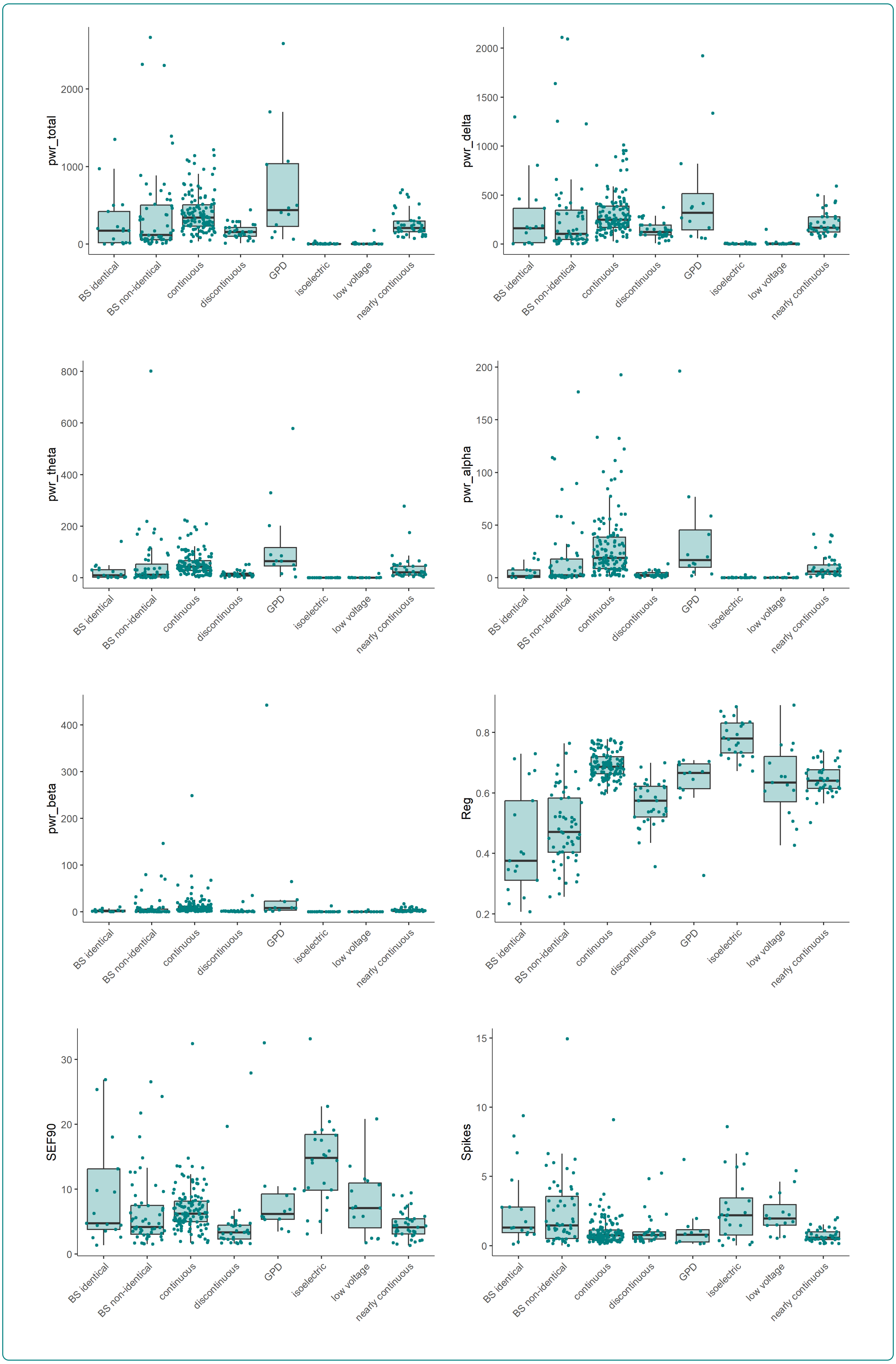


Figure K.18: Feature distribution per electroencephalography (EEG) background category. (n=323)


ESR
1.00
0.75
0.50
0.25
0.00
coh_delta
0.75
0.50
0.25
coh_theta
0.75
0.50
0.25
coh_alpha
0.75
0.50
0.25
coh_beta
0.75
0.50
0.25
AppEn
1.5
1.0
0.5
BS identical
BS non-identical
continuous
discontinuous
GPD
isoelectric
low voltage
nearly continuous


TsEn
0.95
0.90
0.85
0.80
0.75
SpEn
0.80
0.75
0.70
0.65
0.60
0.55
activity
4000
3000
2000
1000
0
mobility
0.75
0.50
0.25
PLI
0.3
0.2
0.1
BSR
1.00
0.75
0.50
0.25
BS identical
BS non-identical
continuous
discontinuous
GPD
isoelectric
low voltage
nearly continuous


pwr_total
0
1000
2000
pwr_delta
0
500
1000
1500
2000
pwr_theta
0
200
400
600
800
pwr_alpha
0
50
100
150
200
pwr_beta
0
100
200
300
400
Reg
0.2
0.4
0.6
0.8
SEF90
0
10
20
30
Spikes
0
5
10
15
BS identical
BS non-identical
continuous
discontinuous
GPD
isoelectric
low voltage
nearly continuous

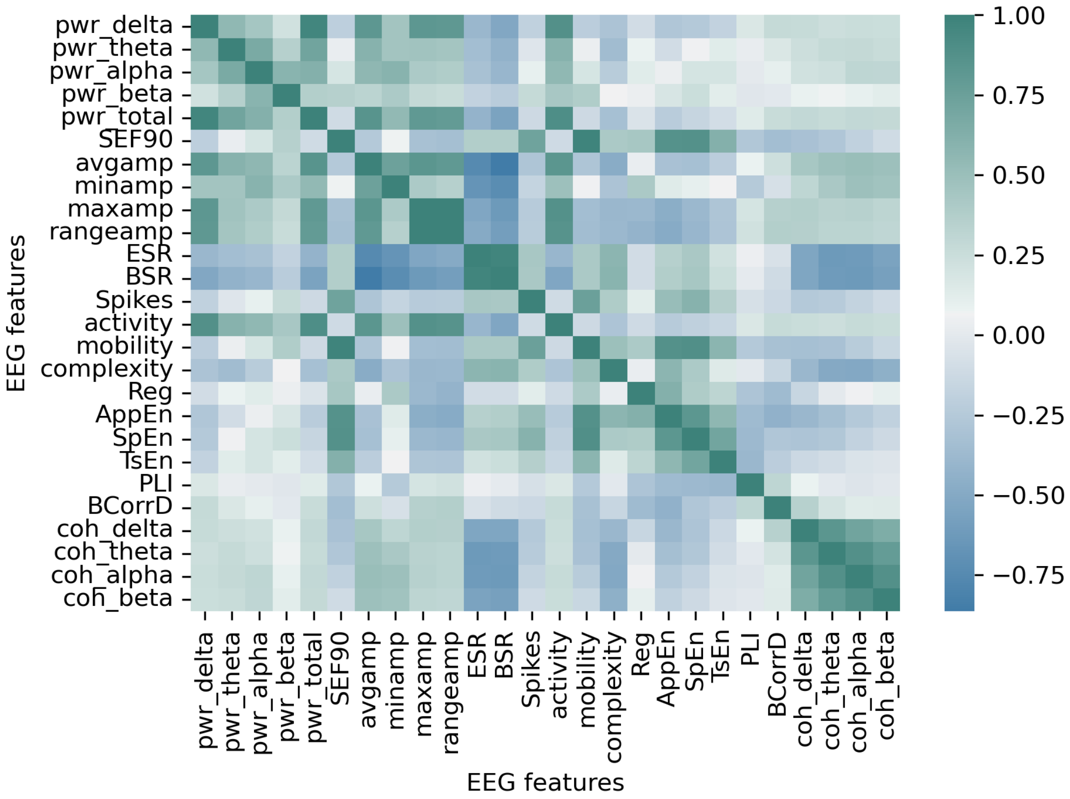


Figure K.19: Correlation heatmap of the different features included in this study. This heatmap illustrates the positive and negative correlations between different electroencephalography (EEG) features. The darker the colour, the stronger the correlation between the features. A teal colour indicates a positive correlation, whereas a blue colour indicates a negative correlation.

L Model development and -evaluation

A common step in the development of machine learning models involves scaling and selecting relevant features. However, in this study, these steps were not undertaken as the Random Forest (RF) algorithm is not sensitive to feature scaling and is less prone to overfitting than other ML models as they consist of multiple decision trees that are trained independently om subsets of the training data. Therefore, the models were developed and trained using the full EEG feature set and the first step in the development of the RF model was hyperparameter tuning. The full model development and -evaluation process is visualised in Figure L.21.

Hyperparameter tuning

Hyperparameters are parameters that are not learned by the model itself but are set prior to training. Tuning hyperparameters involves finding the best combination of values for these parameters to improve the performance of the model. To tune the hyperparameters of the RF classifier, a randomised search with 5-fold cross-validation was performed. Instead of trying all possible combinations of hyperparameter values, which can be computationally expensive, a randomised search randomly samples a subset of hyperparameter configurations for evaluation. Hyperparameters that were used for tuning were:

- **Number of estimators:** integers from 10-300
- **Minimum samples in split:** 2, 5, 10, 15, 20 or 30
- **Minimum samples per leaf:** 1, 2, 3 or 4
- **Criterion:** gini or entropy
- **Bootstrapping:** True or False
- **Max depth of trees:** 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 100

Hyperparameters were tuned based on the 80% traindata of the 5-fold stratified cross-validation on the entire dataset. The best model was used to predict the EEG background category on the 20% set. Eventually leading to a prediction per patient (as all patients are in the test set once).

Reduction of electrodes

The before described approach for model development was repeated for each new EEG montage, meaning that for the all of 5 models that were developed, based on a EEG montage with either 12-, 10-, 8-, 6- or 4- electrodes (Figure L.20) hyperparameter tuning was performed.

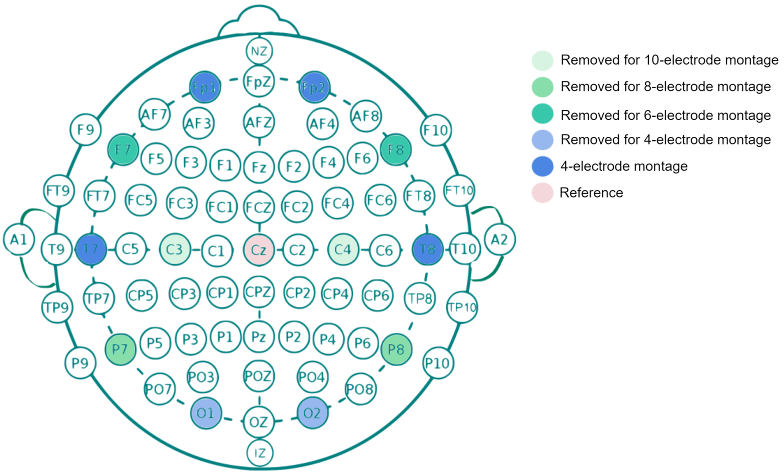


Figure L.20: Electroencephalography (EEG) electrodes used in this study and the reduction of electrodes for the development of different Random Forest classifiers based on input with less electrodes. All filled electrodes were used for the development of the baseline model with 12 electrodes. The colours indicate the stepwise removal of electrodes for montages with 10-, 8-, 6-, and 4 electrodes.

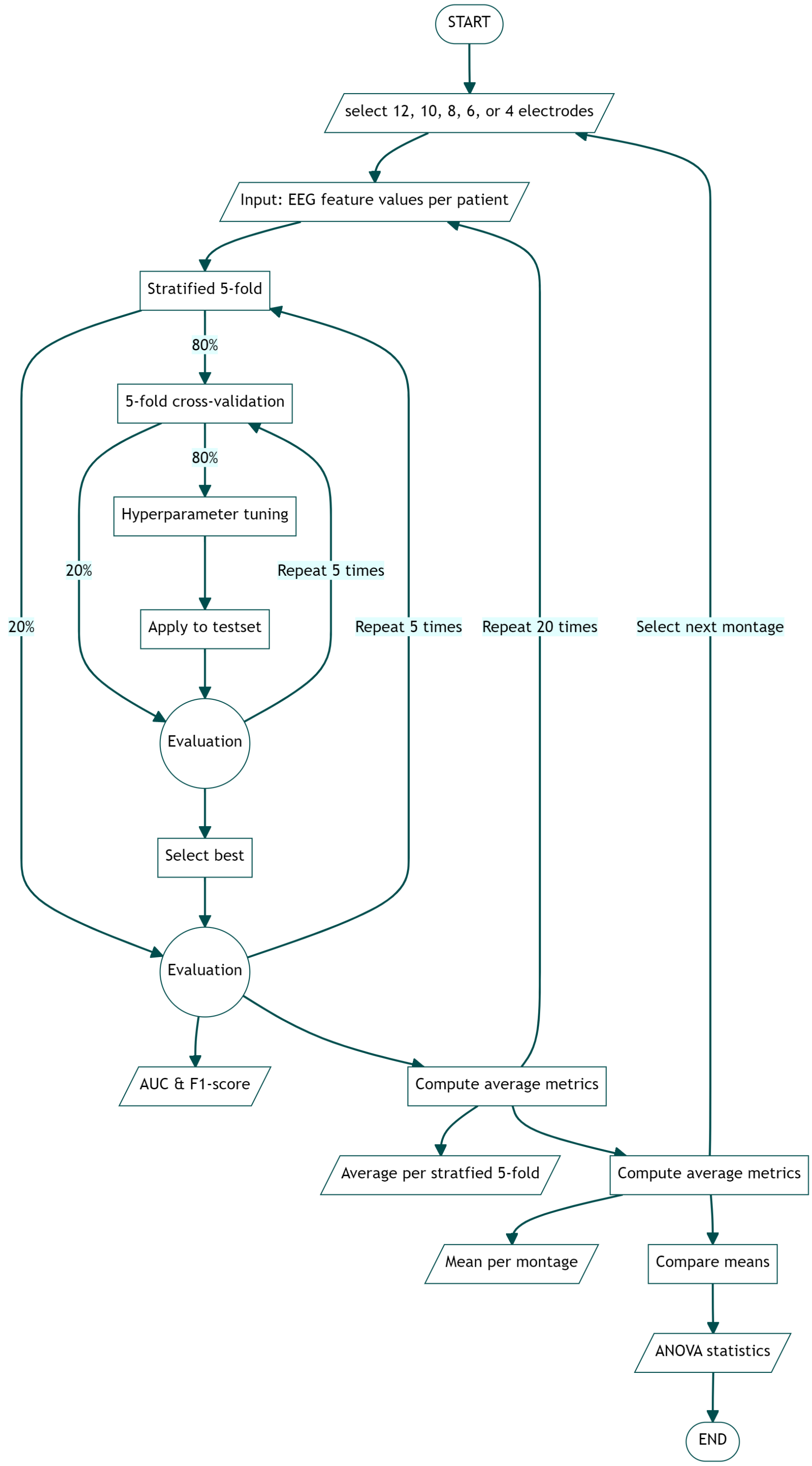


Figure L.21: Code flowchart Random Forest (RF) model development and -evaluation. AUC: Area Under the Curve. ANOVA: ANalysis Of VAriance

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