Stakeholder-led Study Group Application (N-CODE)

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Developing an artificial intelligence framework for identifying people at risk of sudden unexpected death in epilepsy (SUDEP)

Background

Epilepsy is a chronic neurological disorder manifesting as seizures caused by abnormal electrical activity in the brain and affects over 70 million people globally [1]. Sudden Unexpected Death in Epilepsy (SUDEP) is the leading cause of death for people with epilepsy (PWE) but remains poorly understood [2]. It may account for approximately 17–50% of epilepsy-related deaths in the US [3] and 42% in the UK. Between 1999–2017, US epilepsy-related mortality rose by 98.8%, while the UK saw a 69% increase from 2004-2014 [4]. Annually, SUDEP causes about 7,000 deaths in the US and Europe [5]. Total epilepsy costs worldwide reached $119.27 billion [6], while in the UK, the neurological condition had an economic impact of £96 billion in 2019, with epilepsy alone costing the NHS £2 billion annually [7]. With no methods existing to effectively predict or prevent SUDEP risk [8], predicting or preventing SUDEP remains challenging, highlighting the need to understand its etiology and identify risk factors [9]. SUDEP often occurs following a generalised tonic-clonic motor seizure (GTCS), more frequently at night/during sleep [8]. Continuous ECG monitoring for PWE with frequent GTCS can identify high-risk individuals [10]. GTCS are associated with specific EEG patterns reflecting aberrant brain activity during seizures [11]. Artificial Intelligence (AI) is increasingly utilised in healthcare, which can enhance diagnostic accuracy [12].

This study aims to develop an AI model based on identified SUDEP risk markers that can be applied to EEG and ECG recordings to help predict SUDEP risk. To achieve that, our hypothesis is to integrate the changes in both the ECG and EEG during a GTCS in an AI model that might improve the understanding of the etiology of SUDEP and identify its risk markers.

Proof of concept

GTCS has a strong link with distinctive changes in ECG and EEG signals, suggesting the interaction between seizures and autonomic nervous system function. Cardiac changes were observed before death in SUDEP caused by GTCS events [13]. GTCS are associated with specific EEG patterns reflecting aberrant brain activity during seizures. Consequently, ECG and EEG, are essential tools for determining the risk of SUDEP [14].

Questions to be tackled during the meeting: This proposal aims to address the following challenges:

1. **Does the analysis of the GTCS frequencies help to identify the risk factors for SUDEP?**

   We will examine whether the GTCS frequencies is a significant clinical risk factor for SUDEP or not. Some studies have suggested that patients experiencing more than 50 GTCS per year may be more than 14 times more likely to develop SUDEP [15].

2. **Could changes in EEG and ECG signals help with understanding of the etiology of SUDEP and identifying its risk factors?**

   Analysis of changes in EEG and ECG due to SUDEP will be investigated. Some cohort studies showed that ECG monitoring links SUDEP with cardiac dysfunction [18], and EEG monitoring emphasises its role in SUDEP risk assessment [20]. Epilepsy can cause cardiac issues during seizures and interictal periods, leading to functional and structural heart changes. Seizures significantly impact heart rate (HR) [16], which causes EEG abnormalities [17]. While EEG after a seizure, known as postictal global EEG suppression (PGES), has gained interest as it was observed in monitored SUDEP patients at death. Abnormalities after convulsive seizures have been studied as SUDEP risk factors [19].

3. **Is it possible to develop an AI model that helps reduce the fatality rate of SUDEP by identifying its risk factors?**

   We will explore whether it is possible to develop an AI model that can be assisted to reduce the fatality rate of SUDEP by identifying and addressing its risk factors. Early detection of individuals at high risk could enable targeted interventions, potentially lowering the likelihood of SUDEP.

4. **What are the innovative AI techniques that can be investigated to accurately identify individuals at risk of SUDEP based on analysing changes in EEG and ECG signals?**

AI techniques such as machine learning and deep learning to analyse physiological and behavioural data, such as ECG and EEG, to assess SUDEP risk will be examined. Some cohort studies showed that AI techniques to process large datasets, identifying subtle anomalies or changes that may precede seizures or SUDEP events, enabled early detection [21]. The integration of AI with clinical insights offers proactive interventions, improved understanding, and a transformative approach to SUDEP prevention [12].

5. **What is the required level of performance for the developed AI-model to be clinically feasible to identify the risk factors for SUDEP?**

The required levels of accuracy, sensitivity, and specificity for an AI model to be clinically feasible will be examined. Generally, the model must demonstrate high sensitivity and specificity, with accuracy aligning closely to or exceeding current clinical standards. Clinical feasibility also requires robust validation on diverse datasets, reproducibility across populations, and interpretability to ensure trustworthiness. Regulatory guidelines, such as those from the FDA or EMA. Ultimately, the model must significantly improve outcomes, cost-efficiency, or clinical workflow.

6. **What is the available of dataset**

There are many public research datasets available of ECG and EEG for PWE. In addition, collecting EEG and ECG data from two patients to be used for validating the developed AI model.

Required research skills

This project spans multiple disciplines and would gain from a diverse set of expertise in clinical, neuroscience, biomedical data analysis, and AI approaches. Exploring literature and outcomes for other close cohort studies would be useful. But we're very keen on connecting with experts in neurological conditions including epilepsy, cardiologists and neurophysiologists that provide us with deeper knowledge to understand the etiology of SUDEP. Dealing with experts who succeeded in moving their ideas from academic level to the real world would be beneficially. Furthermore, interacting with experts who have knowledge of collecting EEG and ECG from PWE, and experts in AI healthcare technologies, and understanding the needs of stakeholders will be valuable to our project being successful. Integrating experience in multiple disciplines would be crucial to satisfy the project's aim. We have ambitions that N-CODE is a great position to build our team.

Dataset

1. https://physionet.org/content/chbmit/1.0.0/
2. https://biomedepi.github.io/seizure_detection_challenge/dataset/?utm_source=chatgpt.com
3. https://physionet.org/content/siena-scalp-eeg/1.0.0/

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Exploring SUDEP biomarkers from electrophysiological data

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Background and the challenge

Sudden unexpected death in epilepsy (SUDEP) is a leading cause of epilepsy mortality. The mechanisms behind SUDEP are still poorly understood. The main risk factor of SUDEP is poorly controlled generalised seizures. But beyond such clinical risk factor, there are no established quantitative biomarkers of SUDEP.

Previous studies suggested that interictal EEG recordings are altered in SUDEP. Brain networks from EEG data have shown to be associated with seizure propensity, presenting powerful tools to support epilepsy diagnosis and management.
Understanding the role of brain networks in SUDEP is essential to comprehend its mechanisms. Despite some studies indicating that SUDEP is associated to altered connectivity, little is known about the relationship between brain networks and SUDEP.

Networks from peri-ictal EEG and resting-state fMRI imaging were shown to have different properties in SUDEP. Despite the practical limitations of the biomarkers presented in those studies, their results indicate that interictal EEG networks can provide viable biomarkers of SUDEP.

Network-based biomarkers of SUDEP from non-invasive data would allow clinicians to develop optimized personalised care plans to reduce mortality and improve life quality. It would also advance our understanding of the underpinning mechanisms of SUDEP in risk groups (e.g. Dravet syndrome), ultimately supporting the development of preventive intervention.

What data and/or information is available to help address the challenge

At the moment, SUDEP risk in pWE is assessed using standardised questionnaires based on clinical risk factors derived from retrospective studies, and do not give more than a general picture with no weighting attached to the individual risks identified. More specific biomarkers have not been explored in the at risk groups. There is a need for a more objective biomarker to aid in identifying at risk individuals, given that SUDEP accounts for about 600 deaths in the UK each year.

All pWE have EEGs as part of routine diagnostic work up, and many will have more than one recording and occasionally prolonged recordings. Standard EEGs also record a single channel ECG to ensure there is no obvious cardiac rhythm problem present. The raw EEG data on those pWE who have succumbed to SUDEP and any other epilepsy -related death and age matched controls with epilepsy who are still alive will be extracted from existing stored facilities and analysed using AI techniques to explore biomarkers which have been developed by the research team using a population of pWE and have been published elsewhere. The ECG single channel

data from the same EEG recordings will also be analysed, together with any other ECG data that is available in a digital form.

Questions you would like to see tackled during the meeting

- What is the relationship between brain networks and SUDEP?

- Can background EEG and ECG be used to evaluate the risk of SUDEP susceptibility?

- Can biomarkers provide serial information on changing risks?

- Are biomarkers superior to, or complementary to clinical risk factors already identified?

Relevant references

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