Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER324
Topic:	DeltaScan Brain State Monitor for the diagnosis of acute encephalopathy and/or delirium
Summary of findings:	DeltaScan Brain State Monitor is a single-channel beside electroencephalography (EEG) device that aims to determine whether a patient has acute encephalopathy and/or delirium Health Technology Wales researchers searched for evidence on the use of EEG for the diagnosis of delirium. We identified one systematic review that reported on the association of EEG with delirium, one validation study that investigated single-channel EEG for delirium diagnosis, one prospective study that also reported on single-channel EEG and two observational studies that reported on standard EEG as a diagnostic tool. The evidence suggests that EEG is a valuable tool in diagnosing delirium, however whether this is better than standard practice is still unclear. Not all the evidence found reported on single-channel EEG devices of which DeltaScan is an example. However, we did identify three studies that are yet to be published that investigate DeltaScan for the diagnosis of delirium: two randomised controlled trials and one validation study. The evidence from the randomised controlled trials in particular would provide us with more certainty around single-channel EEG compared with standard care. We also did not identify any economic evidence for this topic.

Introduction and aims

Delirium is a common clinical syndrome characterised by disturbed consciousness, cognitive function, or perception, which has an acute onset and fluctuating course. It usually develops over 1–2 days. It is a serious condition that is associated with poor outcomes. However, it can be prevented and treated if dealt with urgently.

Electroencephalography (EEG) is a useful method to understand delirium pathophysiology, but is currently not used as a diagnostic tool. The NICE guideline for delirium prevention, diagnosis and management recommends that if indicators of delirium are identified, a clinical assessment based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria or short Confusion Assessment Method (short CAM) should be carried out to confirm the diagnosis. However, these current screening tools are subjective, and delirium often goes unrecognised which delays treatment.

DeltaScan Brain State Monitor is a single-channel bedside EEG device that determines whether a patient has polymorphic delta waves or not and helps healthcare professionals determine whether their patients have acute encephalopathy or delirium.

Health Technology Wales researchers searched for evidence on the use of EEG for the diagnosis of delirium. We focussed on evidence that included single-channel EEG as this was closest to the new technology DeltaScan.

Evidence overview

This section summarises sources deemed to be most relevant; other sources of evidence identified are listed in the Brief Literature Search Results section for completeness.

We identified one systematic review that reported on the association of EEG with delirium, one validation study that investigated single-channel EEG for delirium diagnosis, one prospective study that also reported on single-channel EEG and two observational studies that reported on standard EEG as a diagnostic tool. We also identified three studies that are yet to be published that investigate DeltaScan for the diagnosis of delirium: two randomised controlled trials and one validation study.

Secondary Evidence

We identified one systematic review that investigated the associations between delirium and EEG measures recorded prior, during and after delirium. The review included a total of 31 studies and the number of participants across studies was 5,609 with a median sample size of 62. The largest study was a randomised controlled trial consisting of 1155 patients. The review reported on different types of EEG. The most frequent diagnostic tools used to assess delirium were the Confusion Assessment Method for the Intensive Care Unit (CAMICU) (16/31 studies) and versions III to V of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (10/31 studies). Boord et al. (2020) found during a delirium episode in adults, EEG slowing was evident, showing its utility in differentiating those with and without delirium. However, it should be noted that none of the studies reporting on 'during delirium' used single-channel electrode devices such as DeltaScan.

Primary Evidence

We identified two post-operative studies that analysed single-channel EEG recordings and compared them against expert delirium diagnoses using the standard tools. The first authors Numan. T et al. (2019) conducted a prospective multicentre study in postoperative patients aged 60 or over (n=159). Before operation and during the first 3 postoperative days, patients underwent a 5-min EEG recording, followed by a video-recorded standardised cognitive assessment. The authors concluded that delirium/possible delirium can be detected in older postoperative patients based on a single-channel EEG recording that can be automatically analysed.

The second study analysed 2 minutes of 321 single-channel EEG recordings of 145 postoperative elderly patients (Hut et al. 2021). Three EEG experts assessed the recordings. The clinical diagnosis of delirium was based on video-recorded standardized cognitive assessments, administered directly after the EEG recording. Different pairs of two clinical experts with at least 5 years of expertise in delirium diagnosis classified each patient independently of each other and unaware of the EEG classification. In cases of disagreement, the third expert was consulted. Hut et al. (2021) reported that a total of 233 assessments (72.6%) showed overlap between the clinical and EEG classifications of the presence/absence of delirium and acute encephalopathy. They concluded that acute encephalopathy in EEG largely overlaps with a clinical diagnosis of delirium. EEG may be sensitive to brain state changes that may not be classified as clinically apparent delirium.

van der Kooi. A et al. (2014) conducted a study to determine the optimal electrode derivation and EEG characteristic to discriminate delirium from no delirium. Standard EEGs were recorded in 28 patients with delirium and 28 age- and sex-matched patients who had undergone cardiothoracic surgery and were not delirious, as classified by experts using Diagnostic and Statistical Manual of Mental Disorders, 4th edition, criteria. The authors found that eyes-closed EEG recording with only two electrodes in a frontal-parietal derivation can distinguish among patients who have delirium and those who do not.

In another prospective study, 200 inpatients undergoing EEG for evaluation of altered mental state were included to determine which findings on routine clinical EEGs correlate with delirium severity across various presentations (Kimchi. E et al. 2019). Patients were assessed for delirium within 1 hour of EEG with the 3-Minute Diagnostic Interview for Confusion Assessment Method (3D-CAM) and 3D-CAM severity score. EEGs were interpreted clinically by neurophysiologists, and reports were reviewed to identify features such as theta or delta slowing and triphasic waves. The authors found the EEG most strongly associated with delirium presence was a composite of generalized theta or delta slowing (odds ratio 10.3, 95% confidence interval 5.3-20.1). Kimchi. E et al. (2019) concluded that generalised slowing on routine clinical EEG strongly correlates with delirium and may be a valuable biomarker for delirium severity.

Ongoing Evidence

We identified three studies which are yet to be published. One study is a prospective multicentre clinical validation study of DeltaScan for the assessment of delirium in ICUs and wards (NCT03966274 2021). Inclusion criteria were patients aged 70 or older, admitted to ICU or ward ICU with a Richmond Agitation-Sedation Scale (RASS) score of -2 or higher. The topic proposer submitted evidence regarding this study that provided further detail: 457 EEG recordings from the two sub-studies were analysed: ICU (n = 206) and ward (n=251). Experienced investigators carried out the DSM-5 criteria on the patients, and the results from this were used along with the patients medical notes by three delirium experts for the diagnosis. These were then compared with the DeltaScan

recordings. The writing of the article is still in progress, however DeltaScan have referenced this study in their 'Clinical Validation Summary' (see 'Evidence submitted by topic proposer' below).

The other two studies identified are both randomised controlled trials in non-ICU and ICU departments. NCT03735940 (2021) is looking to quantify the impact of the use of the DeltaScan on patient outcome (detection rate of delirium and duration of admission) in patients with high risk of delirium compared to the currently used delirium screening tools. The patient population is adults admitted to an intensive care unit (ICU) with high risk of delirium. The second RCT, NCT03735927 (2021), aims to do the same in elderly people admitted to non-ICU departments with high risk of delirium.

Evidence submitted by topic proposer

A Clinical Validation summary was submitted by the topic proposer that summarised results from two trials that we identified in our search and summarised above: Numan. T et al. (2019) and (NCT03966274 2021). In the summary, time to detection benefit was calculated using a parametric, exponential survival model, with results showing that with DeltaScan, estimated time to detection is 1.16 days quicker than patients screened with usual care, with a range of [0.86-1.43] days when extrapolated to day 4 and 6. The summary concludes that in practise, this means that with the EEG-based DeltaScan, more patients with delta activity are found with DeltaScan, typically around 1-1.5 days quicker, and that not all patients show clinical signs of delirium (yet). The summary also pooled data from Numan. T et al. (2019) and NCT03966274 (2021) and showed that for the ward and ICU sub-populations, the results were very similar to the standard clinical references, with consistent overall diagnostic accuracy (AUROC) of over 0.83.

Details of a cost analysis was submitted by the topic proposer. The purpose of the analysis was to estimate the economic benefit of improved delirium detection with the use of DeltaScan compared to usual care. Details of three settings were provided to HTW: ICU, surgery and use of DeltaScan in the frail elderly. The analysis evaluates a closed cohort of patients entering the model in the selected setting and being tested for delirium, and links data from Numan. T et al. (2019) on sensitivity and specificity of each method, with data on the duration of hospitalisation from a literature review. Costs in the model include those associated with the upfront costs of DeltaScan, considering factors such as the lifetime of the device and disposables, nursing and physician costs, hospital stay and costs of multiple component interventions for those patients who are diagnosed with delirium. Across all three provided settings, DeltaScan is shown to be associated with cost-savings of between €399 and €2,500 per patient. Drivers of results are sensitivity and specificity of DeltaScan and Usual Care and hazard ratios applied to the length of stay for patients with early and late detection of delirium.

DeltaScan is a digital health technology and was determined to be a Tier C technology according to the Evidence Standards Framework for Digital Health Technologies**.** Technologies within this classification use data to diagnose a condition in a patient, or to guide a diagnostic decision made by a healthcare professional. For technologies of this classification, the minimum evidence standard is a high-quality intervention study (experimental or quasi-experimental design) showing improvements in relevant outcomes such as diagnostic accuracy and patient-reported outcomes. The best practice standard is a high-quality randomised controlled study or studies done in a setting relevant to the UK health and social care system, comparing the digital health

technology (DHT) with a relevant comparator and demonstrating consistent benefit including in clinical outcomes in the target population, using validated condition-specific outcome measures. Alternatively, a well conducted meta-analysis of randomised controlled studies if there are enough available studies on the DHT.

Areas of uncertainty

The evidence suggests that EEG is a valuable tool in diagnosing delirium, however whether this is better than standard practice is still unclear, and the evidence found did not all use single-channel EEG devices of the type concerned here. These devices are likely to be cost incurring; reduced delirium detection time could offset these costs as demonstrated in the unpublished budget impact model submitted by the topic proposer. However, we did not identify any published economic analysis of DeltaScan or any similar technology. Results from randomised controlled trials that are yet to be published may provide further certainty around this.

Literature search results

Health technology assessments and guidance

NICE. (Updated 2019). Delirium: prevention, diagnosis and management. Clinical guideline [CG103]. doi: https://www.nice.org.uk/guidance/cg103/chapter/1-Guidance

Evidence reviews and economic evaluations

Boord MS, Moezzi B, Davis D, et al. (2020). Investigating how electroencephalogram measures associate with delirium: A systematic review. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology. doi: 10.1016/j.clinph.2020.09.009

Individual studies

Numan. T, Boogaard. M, Kamper. A, et al. (2019). Delirium detection using relative delta power based on 1-minute single-channel EEG: a multicentre study. British Journal of Anaesthesia. 122: 60-8. doi: 10.1016/j.bja.2018.08.021

van der Kooi. A, Zaal. Irene, Klijn. F. (2014). Delirium detection using EEG: what and how to measure? Chest. 147: 94-101. doi: 10.1378/chest.13-3050

Kimchi. E, Neelagiri. A, Whitt. W, et al. (2019). Clinical EEG slowing correlates with delirium severity and predicts poor clinical outcomes. Neurology. 93: e1260-e71. doi: 10.1212/WNL.0000000000008164

Hut SCA, Dijkstra-Kersten SMA, Numan T, et al. (2021). EEG and clinical assessment in delirium and acute encephalopathy. Psychiatry and clinical neurosciences. 75(8): 265-6. doi: https://dx.doi.org/10.1111/pcn.13225

Ongoing research

Clinical Evaluation Program of DeltaScan (ICU)
https://clinicaltrials.gov/ct2/show/NCT03735940

Clinical Evaluation Program of DeltaScan (Ward)
https://clinicaltrials.gov/ct2/show/NCT03735927

Evidence submitted by topic proposer

DeltaScan Validation Study for the Assessment of Delirium in the ICU and on Wards (Val3) https://www.clinicaltrials.gov/ct2/show/NCT03966274

An unpublished 'Clinical Validation Summary' and Budget Impact Model summary was also submitted by the topic proposer.

Date of search:	December 2021
Concepts used:	DeltaScan, one-channel EEG, Delirium, Encephalopathy