Neuronostics

Neuronostics® Platform
Instructions for Use Manual

UK CA

Neuronostics Limited
Engine Shed,
Station Approach,
Temple Meads
Bristol, BS1 6QH

BioEP Instructions for Use Manual Version History

Issue	Date	Revisions
2024.01.1	2023-11-27	Initial release
2024.01.2	2024-01-29	Added SSL validation instructions, refactored release version history to match product versioning
2024.03.1	2024-03-20	Updated support contact details
2024.06.1	2024-06-25	Updated on users creating subject in wrong organisation
2024.11.1	2024.11.21	Update to amend minimum sampling rate to 250 Hz
2024.12.1	2024.12.18	Update to remove references to foreground analysis
2025.01.1	2025.01.09	Add mains interference filtering limitation
2025.02.1	2025.02.27	Update sample BioEP report
2025.06.1	2025.06.18	Added bulk upload section
2025.09.1	2025.09.11	Added information about 'understand this classification' button
2025.11.1	2025.11.03	Added information related to the multi-factor authentication process & the training video

1 TABLE OF CONTENTS

2 INTRODUCTION TO BIOEP

2.1 PRODUCT DESCRIPTION

BioEP Software is a Medical Device (SaMD) intended for analysing **resting-state EEG** collected routinely in clinic from adult patients with suspected epilepsy. BioEP analyses the EEG for the presence of brain network-based markers and data features shown in published literature to be altered in people with epilepsy (Schmidt *et al.* 2016 [1], Chowdhury *et al.* 2014 [2], Woldman *et al.* 2020 [3], Schmidt *et al.* 2014 [4], Tait *et al.* 2023 [5], Kane *et al*. 2017 [6], Kural *et al*. 2020a [7], Kural *et al.* 2020b [8]).

The BioEP analysis provides a single categoric output (i.e. very unsupportive, unsupportive, neutral, supportive, very supportive) that provides an indication of the similarity of a patient's analysed EEG to the EEGs of people who had a suspected seizure, differentiating between cohorts with epilepsy and without epilepsy (including those with alternative conditions such as non-epileptic attack disorder, NEAD).

2.2 INTENDED USE

BioEP is intended to support clinical diagnostic decisions of patients with suspected epilepsy and a clinically non-informative EEG (meaning no epileptiform discharges were observed conclusive for an epilepsy diagnosis). The BioEP report may be used as an aid in the diagnosis of epilepsy or an alternative condition, or to support clinicians in making decisions about the optimal next steps in the care pathway.

BioEP is NOT intended to be used as a standalone diagnostic. It is intended to be used as an additional piece of information in the wider portfolio of evidence used in the clinical diagnosis of epilepsy, or an alternative condition, such as a neurophysiology EEG report and a patient's clinical history. Its key intended benefit is to increase the overall efficiency of the clinical pathway by decreasing time to diagnosis and misdiagnosis rates.

BioEP is intended to be used in clinical settings (primary and secondary care) with a suitable internet connection and web browser requirements (see section 4).

2.3 INTENDED PATIENT POPULATION

BioEP is indicated for use in adults (18+) in the UK referred for an EEG due to a suspicion of epilepsy (regardless of age, gender, treatment status, or comorbidity) by a qualified healthcare professional.

⚠ BioEP should ONLY be used where the clinical query is whether a patient has epilepsy or not.

⚠ BioEP should ONLY be used when the patient is in their baseline state (NOT in a suspected ictal state) when their EEG was taken.

⚠ BioEP should NOT be used in persons with known structural abnormalities or skull breaches, including historical cases, or with people with metal or plastic implants in their brain or skull. The results obtained from such patients are not valid.

2.4 INTENDED USERS AND USE ENVIRONMENT

BioEP is intended for use only by qualified healthcare professionals involved in the epilepsy treatment pathway in clinical healthcare settings. These fall into one of two main user groups of BioEP. These are **Primary and Secondary User Groups** (described below). Each user group contains multiple user profiles:

Primary User – The one who uploads the data for BioEP analysis.

a) clinical neurophysiologists
b) clinical physiologists/clinical scientists (neurophysiology)
c) epilepsy nurses
d) healthcare assistants
e) neurologists/epileptologists
f) research assistants

It's important to note that EEGs uploaded to the platform must be captured by medical professionals with the same level of training required in the standard clinical pathway – this typically means only clinical neurophysiologists or clinical physiologists/scientists.

Secondary User - The one reviewing and consuming the BioEP report. In some cases, this may be the same person as the primary user.

a) neurologists/epileptologists
b) clinical neurophysiologists
c) epilepsy nurses
d) general practitioners (GPs)
e) neuropsychiatrists

To constitute a secondary user, medical practitioners must already have prescribed authority to make clinical decisions in the current clinical pathway.

Where role titles are given above, it is intended that these are industry qualified practitioners with appropriate medical training.

3 CAUTIONS, CONTRAINDICATIONS AND LIMITATIONS

Please carefully read the information in this section before using BioEP, it contains important information on operating safety and correct use of the product.

3.1 CAUTIONS

⚠ A BioEP report is only valid if the EEG data uploaded for analysis was collected by a qualified healthcare professional using an existing UKCA/CE marked medical device hardware, cup electrodes and electroconductive gel or paste. A minimum of 19 scalp electrodes must be placed according to the 10-20 System.

⚠ BioEP can only be used if the file characteristics of the uploaded EEG are consistent with the criteria detailed in Section 8.2.3. [Upload an EEG]. If any of these criteria have not been satisfied, this could lead to an unreliable BioEP output.

⚠ BioEP must only be used on compatible devices (desktop computers and laptops) running compatible up-to-date browsers as detailed in Section 4 [Compatibility]

⚠ BioEP is only to be used in UK adult (18+) patients with suspected epilepsy.

⚠ BioEP is not intended to replace professional clinical judgement; the results must be interpreted by a qualified healthcare professional in the context of wider clinical information such as an EEG report and a patient's clinical history.

⚠ BioEP is a UKCA-marked medical device and is only available for use in the UK.

⚠ BioEP is only intended for use only by qualified healthcare professionals.

⚠ If the neurophysiology EEG contains ictal or interictal epileptiform discharges, the BioEP report is not valid.

3.2 CONTRAINDICATIONS

⚠ BioEP should only be used where the clinical query is whether a patient has epilepsy or not.

⚠ BioEP should only be used when the patient is in their baseline state (NOT in a suspected ictal state) when their EEG was taken.

⚠ BioEP has not been tested in persons with known structural abnormalities or skull breaches, including historical cases, or with people with metal or plastic implants in their brain or skull. The results obtained from such patients therefore are not valid.

⚠ BioEP is NOT to be used as a standalone diagnostic device. Do not rely on the BioEP output alone for starting or adapting epilepsy treatment (which may include administration of anti-seizure medication). Clinical assessment should always lead decisions on patient treatment.

3.3 LIMITATIONS

⚠ BioEP is NOT to be used as a standalone diagnostic but rather as an additional piece of evidence in the wider portfolio of evidence used in the clinical diagnosis of epilepsy, or a differential condition, such as a standard neurophysiology EEG report and a patient's clinical history.

⚠ BioEP is limited to use by qualified healthcare professionals in healthcare settings.

⚠ BioEP is limited to use in UK adult (18+) patients where there is a clinical suspicion of epilepsy.

⚠ BioEP is limited to use on clinically non-informative EEGs, meaning there are no ictal or interictal epileptiform discharges conclusive for an epilepsy diagnosis.

⚠ BioEP is limited to filtering mains interference at frequencies of 50Hz and 60Hz.

4 BIOEP OPERATING PRINCIPLE

4.1 OVERVIEW OF BIOEP OPERATING PRINCIPLE

The BioEP operating principle is described below along with how this integrates into the existing epilepsy care pathway:

1. An EEG is gathered from a patient as part of the existing epilepsy clinical pathway.
2. The EEG data file is exported into a compatible format as detailed in Section 8.2.3. [Upload an EEG].
3. A user then logs into BioEP through the web portal, creates or selects the appropriate patient record and uploads the EEG data file for BioEP analysis.
4. BioEP takes ~ 15 minutes to analyse the EEG; once complete, a BioEP report is made available and stored in the patient's file.

5. The report displays the output category based on the BioEP analysis ready for consumption by a qualified healthcare professional.

Detailed instructions for each step begin in Section 7 [Creating a BioEP report].

4.2 HOW THE BIOEP ALGORITHM WORKS

BioEP uses a suite of algorithms to study the EEG data that has been recorded as part of standard clinical workup. Each algorithm evaluates a specific property of the EEG that has been shown in peer-reviewed literature to be altered in people with epilepsy. We term these digital biomarkers. Similar to physiological biomarkers, like those that can be calculated from blood, the process underpinning each digital biomarker that informs our BioEP rating is fully transparent. The key properties we examine include:

- **2 spectral features:** Peak Alpha Frequency & Alpha Power.

- **4 Brain network features:** The brain functions as a network of interconnected regions that constantly communicate with each other. BioEP uses concepts from *graph theory* to assess the structure and strength of these connections, providing an indication of how different brain regions interact. We specifically look at Mean Degree, Degree Variance, Clustering Coefficient & Characteristic Path-Length.

- **2 model based features:** Our understanding of how seizures emerge in the brain from apparently normal brain states has grown rapidly in recent years. It is now understood that the interplay between brain networks and the dynamics they support are critical ingredients for seizures to occur. To assess this BioEP uses concepts from *mathematical modelling.* Essentially, we construct a computer representation of brain networks, informed from the networks inferred from the collected EEG. The computer model is a set of *differential equations*, these describe how brain dynamics vary over time. Simulations of these models under a variety of conditions rapidly reveal the ease with which seizures can emerge. Parameters that charactertise this ease from a modelling perspective provide the final biomarkers (called local and global coupling) used to inform the BioEP rating.

All our biomarkers are rooted in the following published scientific literature: Schmidt *et al.* (2016) [1], Chowdhury *et al.* (2014) [2] Woldman *et al.* (2020) [3] and Schmidt *et al.* (2014) [4].

Warning: BioEP's algorithms are designed with the critical assumption that the EEG is recorded during a resting state. If the EEG reflects a seizure state (e.g., the presence of epileptiform discharges indicative of an epilepsy diagnosis), this assumption is violated. In such cases, BioEP is not suitable for use.

Following feature extraction, the biomarkers are input into statistical models (random forest and logistic regression). By combining the model outputs, a single categoric result (e.g. supportiveness of epilepsy) is constructed. This category output is an indication of the similarity of the analysed EEG to the EEGs of people who had a suspected seizure, differentiating between cohorts with confirmed epilepsy and those confirmed not to have epilepsy (including those with a differential condition).

5 COMPATIBILITY

5.1 COMPATIBLE DEVICES

The Neuronostics Platform is only designed for use on desktop computers or laptops. It is NOT designed to be accessed from mobile devices or tablets.

5.2 COMPATIBLE BROWSERS

The Neuronostics Platform is compatible with the following browsers when run on Microsoft Windows 10 or greater:

- Google Chrome
- Microsoft Edge

  In both cases, the latest versions are recommended, but releases from within the past 12 months are supported.

The Neuronostics Platform must be run on a stable internet connection of at least a 10MB upload and 10MB download speed.

6 TRAINING

When you first use the Neuronostics Platform (as well as after major updates) you will be required to complete the BioEP training which includes:

- Reviewing the BioEP instructions for use manual in full
- Watching the mandatory BioEP training video

Checking the box upon first sign-in will confirm you've been trained and will be stored by the platform as evidence that you completed the training.

7 GETTING STARTED

To start using BioEP, you need a personal Neuronostics Platform account. Setting up an account can be achieved in a few simple steps. Follow the step-by-step instructions below to get started with an account.

7.1 INVITES

Your IT department has the ability to administer new invites to the Neuronostics Platform. Please contact them to request an invitation.

Upon receiving an invitation, the link in the email should be clicked and the form filled out to create an account.

7.2 LOGGING IN

Whenever you need to access the Neuronostics Platform (BioEP), login by visiting:

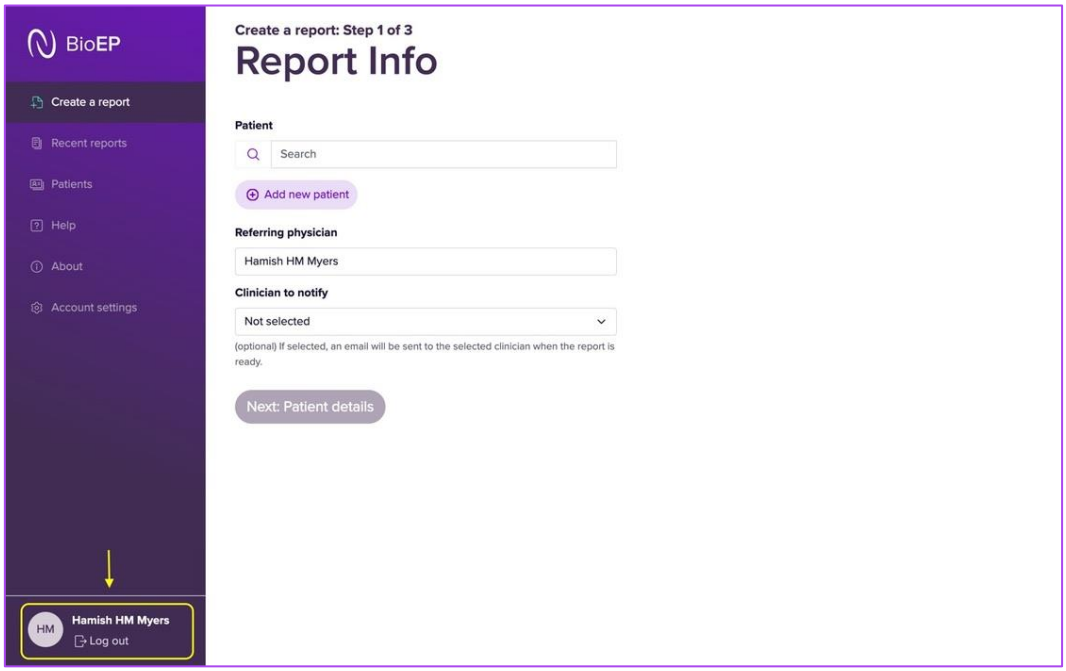
https://uk-healthcare.neuronostics.com/

7.3 RESETTING PASSWORD

If you forget your password or want to reset it, click the “forgot your password” link on the login page and follow the on-screen instructions to receive an email link to set a new password.

7.4 LOGGING OUT

You can log out any time by clicking the logout button at the bottom left of the screen (in the navigation sidebar) as seen in the image below:



7.5 AUTO-LOGOUT

For additional security, the Neuronostics Platform has an inactivity timeout after 15 minutes which will automatically log you out. To continue where you left off, log back in and you'll be redirected to the same page that you were previously viewing.

7.6 UPDATING ACCOUNT DETAILS

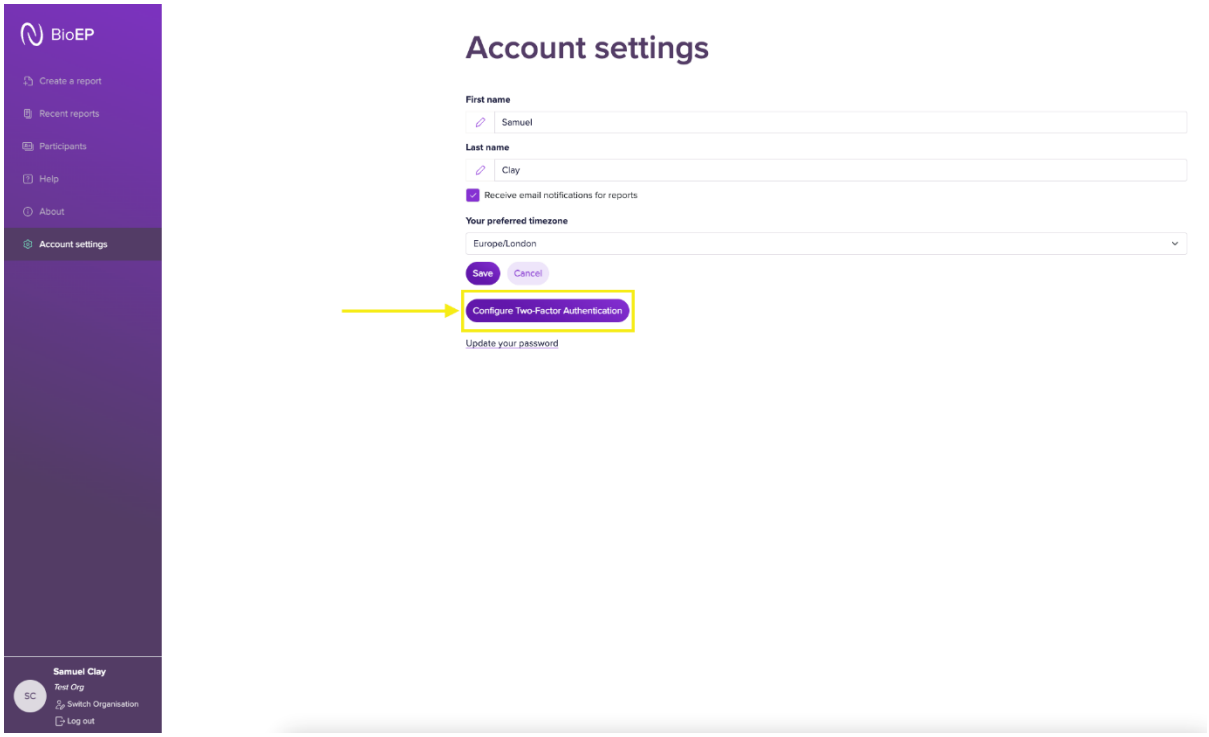
Your account details can be updated at any time by clicking on your name in the bottom left of any screen and then editing any available details. Your email address cannot be changed directly. To do so, you will need to contact help@neuronostics.com or submit a request via our questions and feedback form.

7.7 BLOCKED ACCESS

If you have several failed attempts at your password, you will have to wait for 5 minutes as a cooling off period before trying again. If you continue to input your password incorrectly your account may be blocked. In this eventually, contact help@neuronostics.com for help or submit an issue via our issue form.

7.8 MULTI-FACTOR AUTHENTICATION

You can configure Multi-Factor Authentication (MFA) on your account to use either a token via a token generator app or via a token to your e-mail, to add an additional authentication step after signing in with your username and password. To set this up, go to the 'Account settings' page and click 'Configure Two-Factor-Authentication' as seen in the image below. From there, follow the on-screen instructions to complete the setup process.



8 CREATE A SINGLE BIOEP REPORT

Requesting a BioEP analysis and receiving a BioEP report involves 3 simple steps:

Step 1. Select/create a patient profile and add report information
Step 2. Add additional patient details (i.e. confounders)
Step 3. Upload the EEG for BioEP analysis

This process is explained in the following steps.

Note: Only “primary” users are able to upload data to the platform and create BioEP reports, whilst “secondary” users are able to read reports. Some users will be both “primary” and secondary “users” allowing them to create reports and read reports.

8.1 STEP 1: INPUTTING REPORT INFORMATION

After logging in, click “Create a report” on the left-hand navigation menu and you will be taken to step 1 (of 3) for creating a BioEP report. This step involves inputting the report information.

In this step, first create or select a patient profile by:

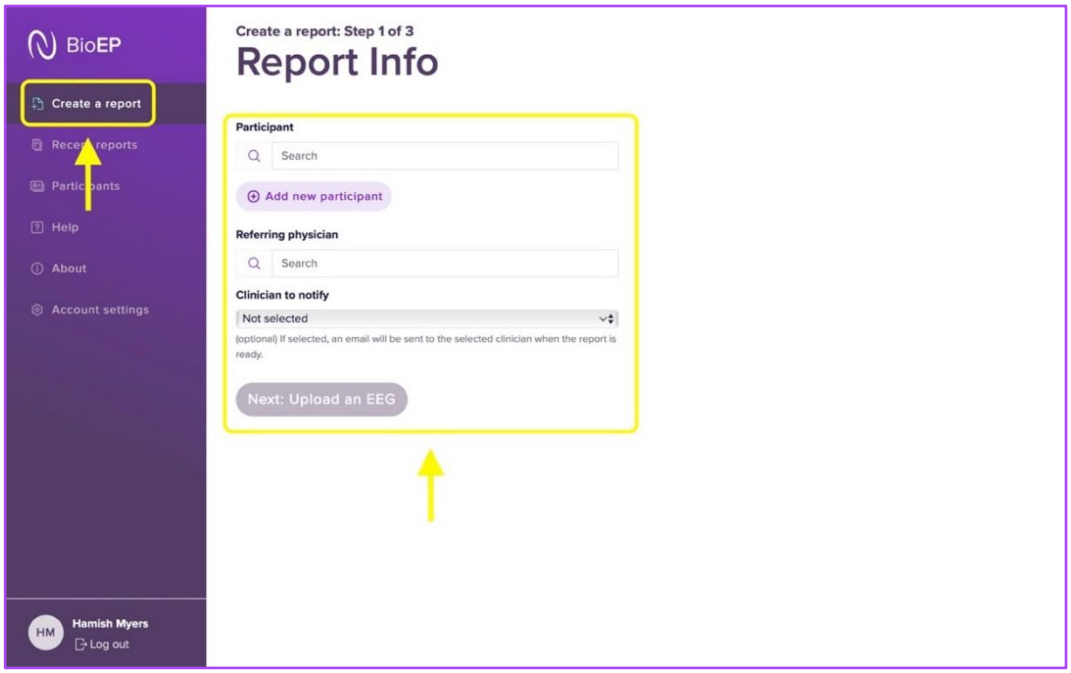
a. Clicking “Add new patient” and entering the patient details in the fields provided. (You will see an error if the patient already exists)
b. Searching for an existing patient (if a patient already exists, it will appear below the search box as you type it in)

When creating a patient, should you become aware that the patient has been created in the wrong organisation, you should email help@neuronostics.com

Once a patient is selected or created, a summary of the patient's information including name, date of birth and NHS number will appear in a summary box on screen. Please always double check this information is correct against your own records.

(Optional) There is an option to select the referring clinician (this is the clinician that requested the EEG). If this is unknown, leave it blank.

(Optional) There is also option to elect a clinician to notify by email when the report is ready.



Once the report information is added, press the "add patient details button" to move to step 2 (of 3).

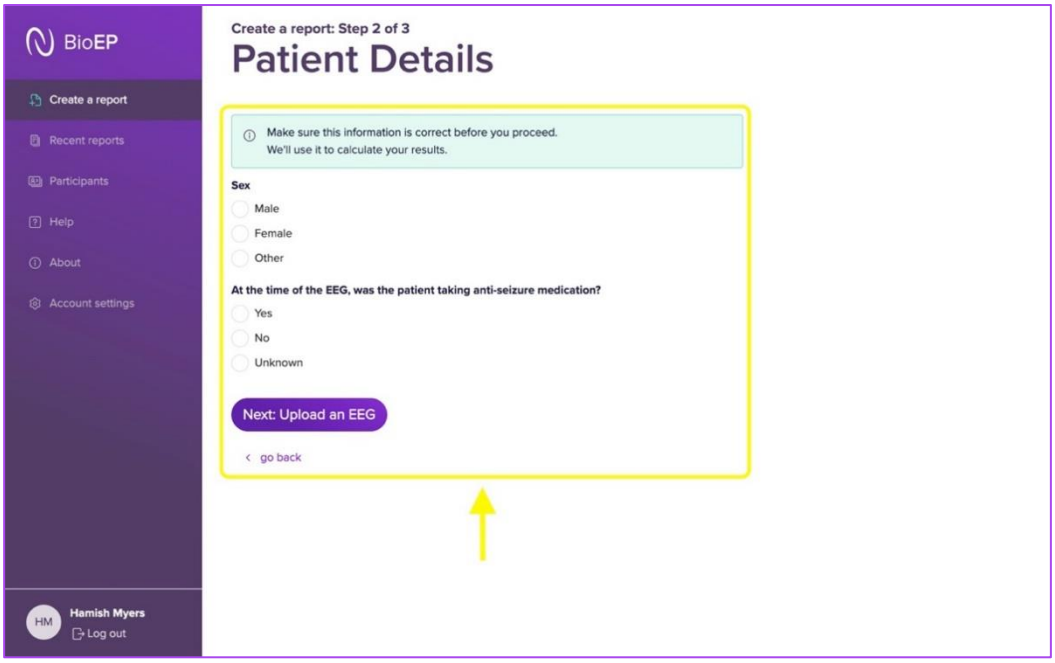
8.1.1 EDITING A PATIENT PROFILE

To edit a patient's profile details, click on the patients' tab on the left-hand navigation panel. Then search for the patient you are looking for. Click on the patient profile. In the top right you will see a button that says edit patient, from here you can edit all relevant patient details.

8.2 STEP 2: ADDING PATIENT INFORMATION (CONFOUNDING VARIABLES)

On step 2 (of 3), select the patient's sex at birth (if known) and input if they were taking a prescribed anti-seizure medication (ASM) at the time of their EEG (if known). Both factors will be considered and will help to provide a **more accurate BioEP analysis.**

Once these details are added, move to step 3 (of 3) by pressing the 'upload an EEG' button.



8.3 STEP 3: UPLOAD AN EEG

To upload an EEG, it must first be first exported from your EEG software as an EDF (European data format) file. The instructions for how to do this will be found in the instructions for your EEG software.

To function correctly, BioEP requires that EEGs follow these criteria of requirements:

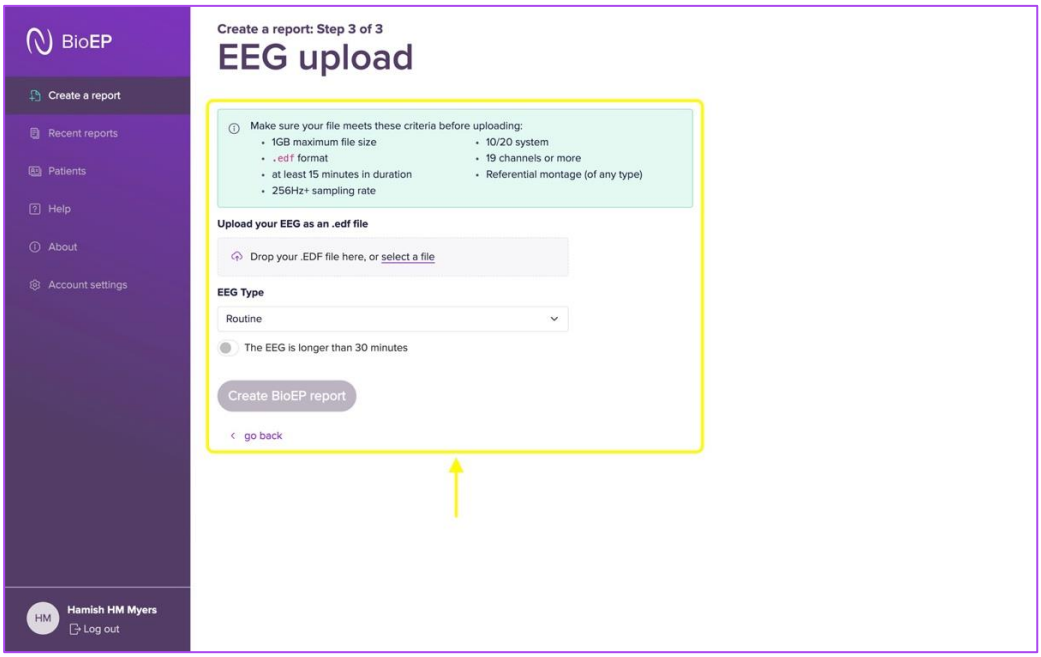
- .edf format
- 1GB maximum file size
- at least 15 minutes in duration (comprising awake and preferably relaxed, eyes closed)
- >= 250Hz sampling rate
- 10-20 system or Modified Maudsley
- 19 channels or more
- Exported in referential montage (of any type)

⚠ A BioEP report is only valid if the EEG data uploaded for analysis was collected by a qualified healthcare professional using an existing UKCA/CE marked medical device hardware, cup electrodes and electroconductive gel or paste. A minimum of 19 scalp electrodes must be placed according to the 10-20 System or Modified Maudsey.

When your EEG file is ready, click the box to select the file from your computer or simply drag it on to the upload box. An upload progress bar will show to indicate the upload progress.

Once the file has uploaded, click the “Process EEG” button. You will now be taken to a processing wait screen.

It usually takes approximately 15 minutes for BioEP to analyse an EEG. You do not have to wait on this screen, a report will be made available when the analysis is complete.

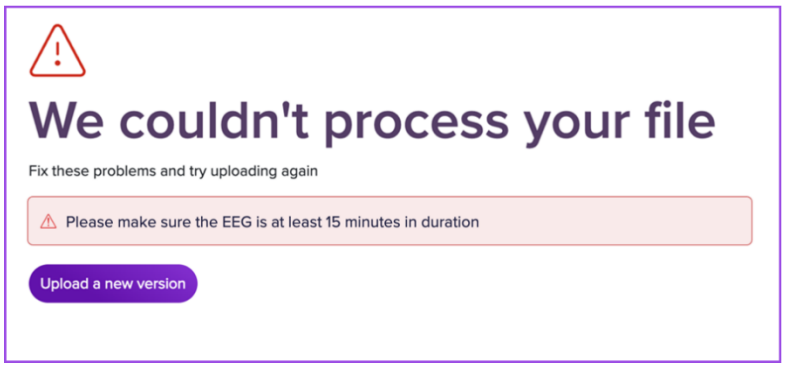


8.3.1 PRUNE THE DURATION OF AN EEG

Should you export and upload a longer duration EEG (over 30 minutes), it’s possible to trim the duration of that EEG to select the portion which you want to submit for analysis. To access this option, simply click the checkbox labelled “The EEG is longer than 30 minutes” and then input the time offsets for the start and end of the section you would like BioEP to analyse.

8.3.2 UPLOAD ERRORS

There may be instances when an uploaded file cannot be processed, either due to a problem with the uploaded file, or due to an internal error. In these cases, the processing screen will describe the error in detail and explain how to resolve it. An upload error may look like:



For internal errors, the Neuronostics Team will investigate as soon as possible and get back to you. If an EEG has been processing for more than 24 hours, please contact help@neuronostics.com or submit an issue via the raise an issue form and reference the unique report ID displayed in the report and we will investigate the issue.

8.3.3 FILE INTEGRITY CHECKING

It is a requirement that the .edf files uploaded are retained on your internal systems since they will be required in the event that you want to cross-check which file was used to create a particular BioEP report.

Your IT department has the ability to help check which file was used to create a particular BioEP report. Contact your IT department for support with these instances.

8.4 FINDING A BIOEP ANALYSIS REPORT

There are multiple ways to find patients' BioEP reports. The first way is to search through your recent reports tab which can be found in the navigation panel on the left-hand side of the screen (more detail below). The second way is to search through the patients' tab which can also be found in the navigation panel on the left-hand side of the screen (more detail below)

8.4.1 FINDING A REPORT FROM RECENT REPORTS

The recent reports section details recently created reports and their status, both for your own uploads, and for those from the whole organisation you belong to. The screen presents a filter option which can be used to toggle between only seeing only your reports and seeing all the reports for the organisation.

8.4.2 FINDING A REPORT FROM A PATIENT

An alternative method to find a report is to visit the "Patients" section from the left-hand menu and type the participant's name in the search box. This screen will update as you type, and you can click through to the patient you wish to view. You can search by patient name, date of birth or NHS number.

8.5 PDF DOWNLOAD

A PDF download of any BioEP report can be obtained by clicking the download button in the top right corner of the online view of the BioEP report. This report is an exact copy of the online version and can be used to store in the patient's medical record.

9 CREATE MULTIPLE BIOEP REPORTS THROUGH BULK UPLOAD

If enabled for your organisation on the BioEP platform you will be able to upload and process EEGs in bulk. If you do not see the bulk upload options, please reach out via help@neuronostics.com or the help centre (on the left-hand navigation menu on the platform).

9.1 UPLOADING MULTIPLE EEGs

After logging in, click "Bulk upload" on the left-hand navigation menu and you will be taken to the bulk upload page. From this page you will be able to upload either a compressed ZIP file containing your EEGs or select multiple .edf files for processing.

Whether uploading a ZIP file or multiple .edf files, the files need to meet the same criteria as when uploaded individually (see section 8.3 for criteria). Additionally .edf files uploaded via bulk upload must be named in a specific format to allow extraction of the necessary information for processing.

File naming format: [Patient ID]_[Sex]_[ASM].edf

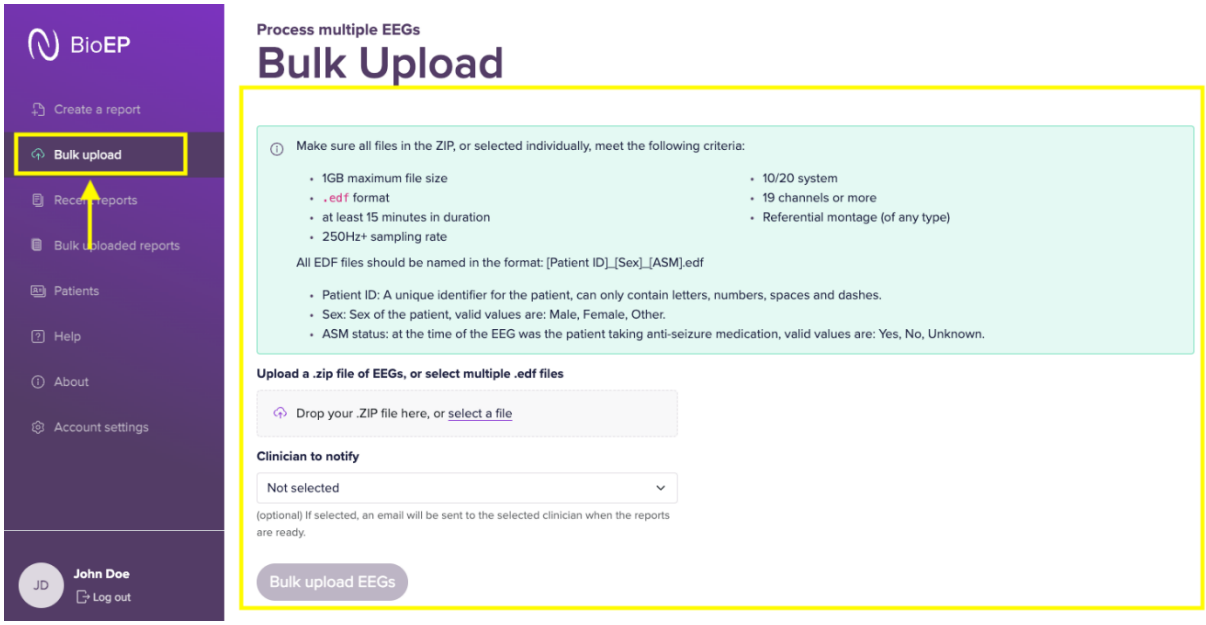
- Patient ID: A unique identifier for the patient, can only contain letters, numbers, spaces and dashes. Will be used to link the .edf record to an existing patient in the platform where the identifier already exists or to create a new patient.
- Sex: Sex of the patient (at birth), valid values are Male, Female or Other. Used as part of the confounding variables for analysis.
- ASM status: at the time of the EEG was the patient taking anti-seizure medication, valid values are Yes, No or Unknown. Used as part of the confounding variables for analysis.

When your ZIP file or multiple .edf files are ready, click the box to select from your computer or simply drag it on to the upload box. An upload progress bar will show to indicate the upload progress.

(Optional) There is also option to elect a clinician to notify by email when the reports from the bulk upload are ready.

Once the ZIP file or multiple .edf files have uploaded, click the “Bulk upload EEGs” button. You will now be taken to a processing wait screen.

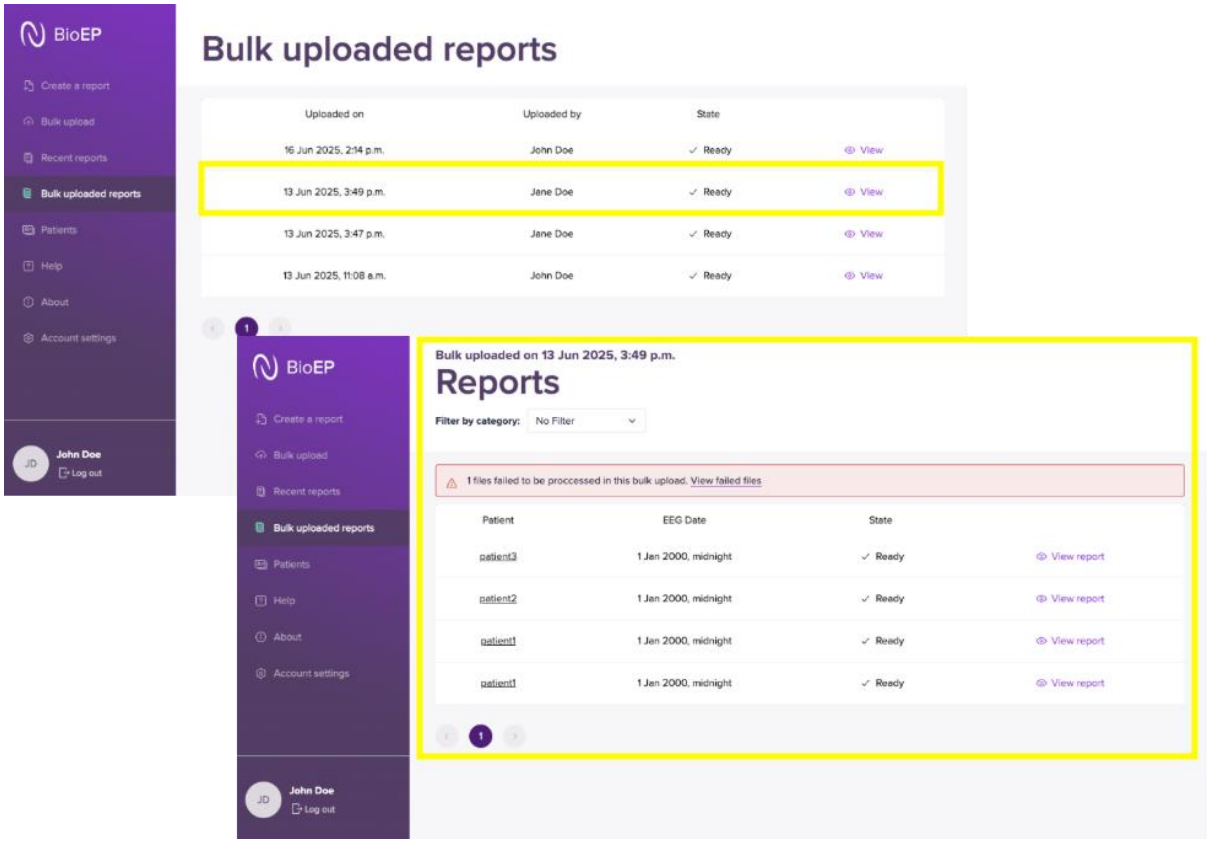
Bulk uploads can take some time depending on how many EEGs there are to process. You do not have to wait on this screen, a report will be made available when the analysis is complete via the Bulk uploaded reports page.



9.2 FINDING REPORTS FROM A BULK UPLOAD

After logging in, click “Bulk uploaded reports” on the left-hand navigation menu and you will be taken to the bulk uploaded reports page. This page details the bulk uploads that have been created along with their status. For each bulk upload that has been added to the system you are able to click through and view the reports associated with that upload. Details of any file that failed to be processed in the bulk upload will also be present on this page.

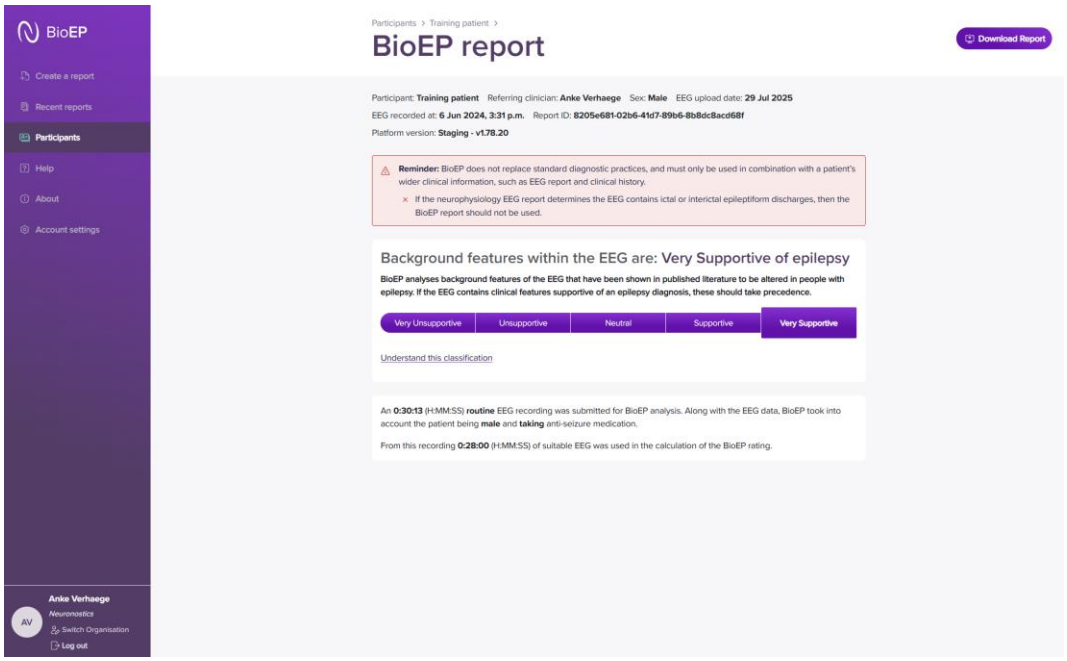
Note: Bulk uploaded reports can still be found and viewed via the patient page see section 8.4.2



10 USING THE BIOEP REPORT TO INFORM A CLINICAL DECISION

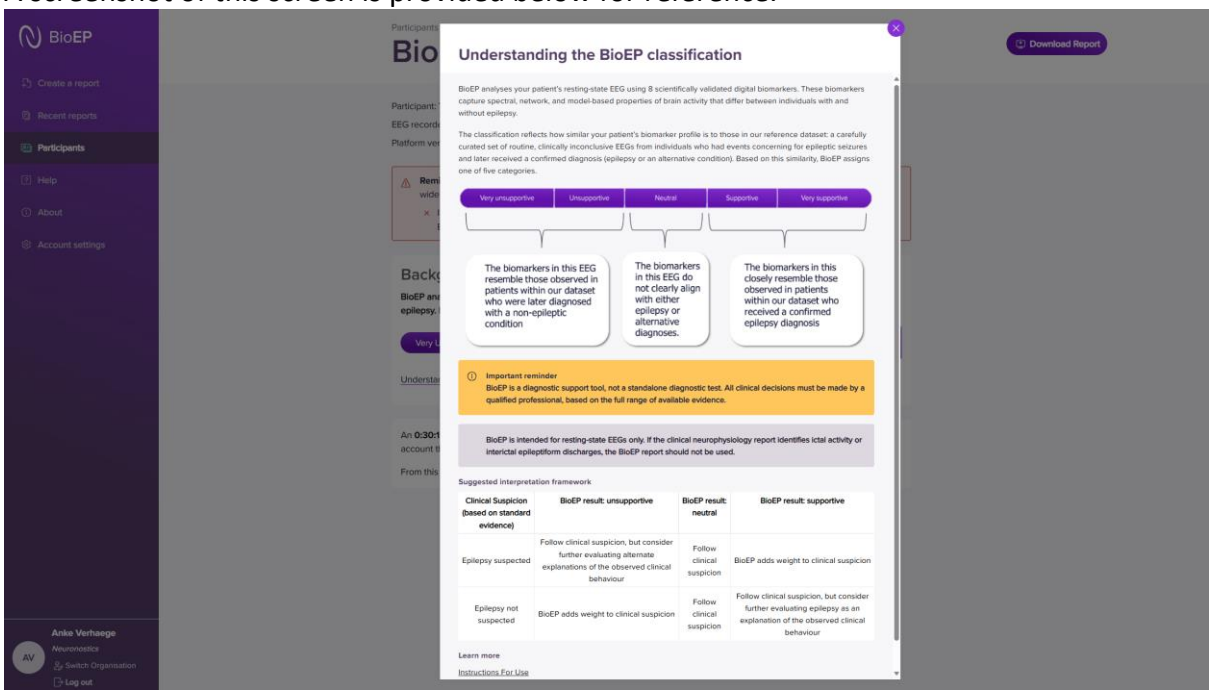
10.1 WHAT'S INCLUDED IN THE BIOEP REPORT

Below you can find a sample BioEP report.



Note the unique BioEP report ID and the BioEP version. These will both be required when reporting an issue about a report to help@neuronostics.com / via the raise an issue form.

When clicking the **"Understand the Classification"** button, a modular screen will open, providing the clinician with additional information on the meaning of the BioEP score. This includes a suggested interpretation framework to support clinical decision-making.
A screenshot of this screen is provided below for reference.



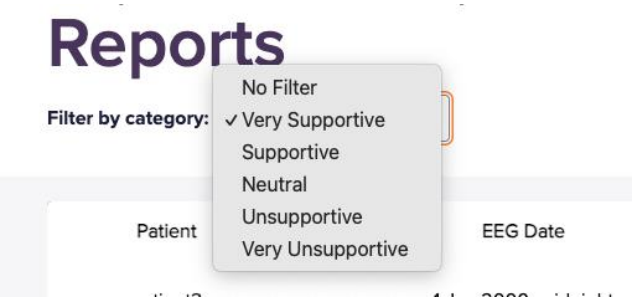
10.2 THE BIOEP OUTPUT CATEGORIES

The BioEP analysis provides a BioEP category based on a 5-point Likert scale from very unsupportive to very supportive of epilepsy. The greater the presence of the digital biomarkers BioEP uses in its analysis which have been shown to be elevated in people with epilepsy as described in Tait *et al.* (2023) [5] the greater the supportiveness of epilepsy and the higher the corresponding BioEP category. Table 1 explains the technical meaning of BioEP's 5-point category scale.

5-point scale in the BioEP report	Technical meaning of the BioEP output categories
Very Unsupportive	The biomarkers in this EEG closely resemble those observed in patients within our dataset who were later diagnosed with a non-epileptic condition.
Unsupportive	
Neutral	The biomarkers in this EEG do not clearly align with either epilepsy or alternative diagnoses.
Supportive	
Very Supportive	The biomarkers in this EEG closely resemble those observed in patients within our dataset who received a confirmed epilepsy diagnosis.

Table 1: The BioEP category scale

Note: reports can be filtered by their BioEP output categories on the recent reports page and from a bulk upload reports page.



10.3 SUGGESTED CLINICAL INTERPRETATION

BioEP should ONLY be used in addition to standard diagnostic practices of epilepsy and in the case of a non-informative EEG, meaning there are no epileptiform discharges observed conclusive for an epilepsy diagnosis. The BioEP report is just one piece of evidence in a wider portfolio of evidence that a clinician may use in making clinical diagnostic decisions, or when deciding the appropriate next steps for a patient who presented at clinic with suspected epilepsy. In the case of epilepsy, this wider portfolio of evidence typically includes a standard neurophysiology EEG report and a patient's clinical history. In the absence of either of these pieces of information, BioEP should not be used.

Table 2 indicates how the additional information from the BioEP report can be used with other existing clinical information to inform a clinical decision.

	BioEP result negative unsupportive of epilepsy	**BioEP result neutral**	**BioEP result positive supportive of epilepsy**
Standard clinical evidence creates clinical suspicion of epilepsy	Follow clinical suspicion, but consider further evaluating alternate explanations of the observed clinical behaviour	Follow clinical suspicion	BioEP adds weight to clinical suspicion
Standard clinical evidence creates clinical suspicion of NOT epilepsy	BioEP adds weight to clinical suspicion	Follow clinical suspicion	Follow clinical suspicion, but consider further evaluating epilepsy as an explanation of the observed clinical behaviour

Table 2: Suggested clinical interpretation for combined standard clinical evidence and BioEP report

Table 2 indicates that, especially when there is a difference in the clinician's suspicion of epilepsy drawn from standard clinical evidence and the BioEP output category, the combination aids the clinician in finding the correct diagnosis either by adding weight to the

clinician's suspicion or by suggesting the need for further evaluation of alternative explanations and/or the need to investigate further with additional tests.

11 NOTIFICATIONS

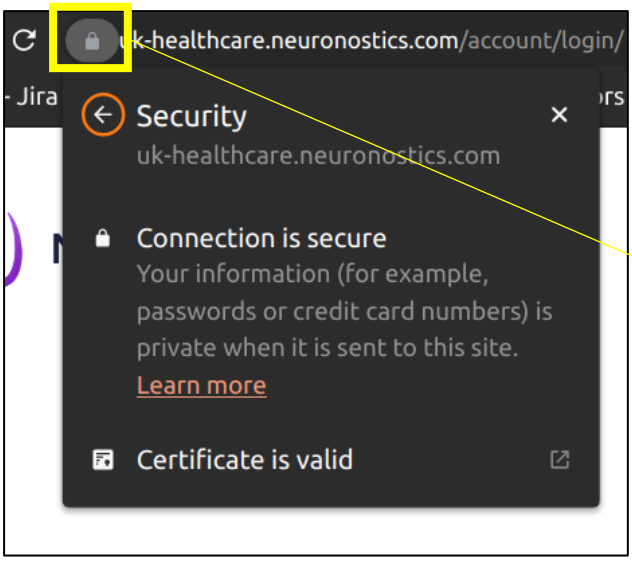
BioEP has the ability to notify you, or relevant clinicians (that you can select when uploading an EEG) via e-mail when a BioEP report is ready or if any issues have been encountered with your uploaded EEG during the BioEP analysis.

You can update your email notification preferences at any time by clicking on your name in the bottom left of any screen.

12 TROUBLESHOOTING AND MAINTENANCE

12.1 HOW TO ENSURE A SECURE CONNECTION

It's possible to ensure you have a secure connection to the platform from within your web browser by clicking on the padlock icon to the left of the web address at the top of the screen, which will show a popup similar to the following image:



Use this if you are not confident that you are connected to the correct server. The web address should always be "uk-healthcare.neuronostics.com".

12.2 OUTAGES

Information about any ongoing issues or outages affecting the Neuronostics platform can be found at the following link:

https://status.uk-healthcare.neuronostics.com/

The page is updated live and will be the primary means by which our support team will update you in the event of any incidents and alert you when the platform is available to use again.

12.3 SCHEDULED MAINTENANCE

Any scheduled maintenance will be conducted outside of regular working hours and will be minimised. It will be advertised on the status page (link in previous section).

12.4 URGENT INFORMATION MESSAGES

Should there be any other urgent information which will affect your ability to use the Neuronostics platform as you'd expect, the Neuronostics team will add a banner message at the top of all pages.

13 CONTACT DETAILS AND SUPPORT

For more information or questions, or for any additional support for BioEP please contact:

help@neuronostics.com

Serious incidents that have occurred in relation to the device must be reported to Neuronostics also via the same email address.

14 APPLICABLE SYMBOLS

Product Name: BioEP

Software Version: V2025.11.1

Manufacturer Address: Neuronostics Limited, Engine Shed, Station Approach, Temple Meads, Bristol, BS1 6QH

Release date: 2025-11-05

Caution: please pay careful attention to information presented with this symbol

15 APPENDIX

15.1 LINK TO SCIENTIFIC REFERENCES

[1] Schmidt, H., Woldman, W., Goodfellow, M., Chowdhury, F. A., Koutroumanidis, M., Jewell, S., Richardson, M. P., & Terry, J. R. (2016). A computational biomarker of idiopathic generalized epilepsy from resting state EEG. Epilepsia, 57(10), e200–e204. https://doi.org/10.1111/epi.13481

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5082517/

[2] Chowdhury FA, Woldman W, FitzGerald THB, Elwes RDC, Nashef L, et al. (2014) Revealing a Brain Network Endophenotype in Families with Idiopathic Generalised Epilepsy. PLOS ONE 9(10): e110136. https://doi.org/10.1371/journal.pone.0110136

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110136

[3] Woldman, W., Schmidt, H., Abela, E. et al. Dynamic network properties of the interictal brain determine whether seizures appear focal or generalised. Sci Rep 10, 7043 (2020). https://doi.org/10.1038/s41598-020-63430-9

https://www.nature.com/articles/s41598-020-63430-9 –

[4] Schmidt H, Petkov G, Richardson MP, Terry JR (2014) Dynamics on Networks: The Role of Local Dynamics and Global Networks on the Emergence of Hypersynchronous Neural Activity. PLOS Computational Biology 10(11): e1003947. https://doi.org/10.1371/journal.pcbi.1003947

https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1003947

[5] Tait, L., Staniaszek, L., Galizia, E., Martin-Lopez, D., Walker, C., Abdul Azeez, A., Meiklejohn, K., Allen, D., Price, C., Georgiou, S., Bagary, M., Khalsa, S., Manfredonia, F., Tittensor, P., Lawthom, C., Shankar, R., Terry, J., & Woldman, W. (2023). Estimating the likelihood of epilepsy from clinically non-contributory EEG using computational analysis: A retrospective, multi-site case-control study. *medRxiv.* https://doi.org/10.1101/2023.03.08.23286937

https://www.medrxiv.org/content/10.1101/2023.03.08.23286937v2

[6] Kane N, Acharya J, Benickzy S, Caboclo L, Finnigan S, Kaplan PW, Shibasaki H, Pressler R, van Putten MJAM. A revised glossary of terms most commonly used by clinical electroencephalographers and updated proposal for the report format of the EEG findings. Revision 2017. Clin Neurophysiol Pract. 2017 Aug 4;2:170-185. doi: 10.1016/j.cnp.2017.07.002. Erratum in: Clin Neurophysiol Pract. 2019 Jun 15;4:133. PMID: 30214992; PMCID: PMC6123891.https://doi.org/10.1101/2023.03.08.23286937

https://pubmed.ncbi.nlm.nih.gov/30214992/

[7] Kural MA, Duez L, Sejer Hansen V, Larsson PG, Rampp S, Schulz R, Tankisi H, Wennberg R, Bibby BM, Scherg M, Beniczky S. Criteria for defining interictal epileptiform discharges in EEG: A clinical validation study. Neurology. 2020 May 19;94(20):e2139-e2147. doi: 10.1212/WNL.0000000000009439. Epub 2020 Apr 22. PMID: 32321764; PMCID: PMC7526669.

https://pubmed.ncbi.nlm.nih.gov/32321764/

[8] Kural MA, Tankisi H, Duez L, Sejer Hansen V, Udupi A, Wennberg R, Rampp S, Larsson PG, Schulz R, Beniczky S. Optimized set of criteria for defining interictal epileptiform EEG discharges. Clin Neurophysiol. 2020 Sep;131(9):2250-2254. doi: 10.1016/j.clinph.2020.06.026. Epub 2020 Jul 17. PMID: 32731161.
https://pubmed.ncbi.nlm.nih.gov/32731161/

END OF IFU