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EpiCARE – a network for rare and complex epilepsies

HP-ERN-SGA-2018 European Reference Networks / Framework Partnership Agreement

D3.1 Summary of recommendations for neuroimaging in epilepsy in general, and in specific patient populations (e.g. presurgical imaging) and the creation of imaging databases

1. Introduction

Neuroimaging WP set out to promote harmonisation of best practices in neuroimaging evaluation of rare and complex epilepsies to enable state-of-the-art procedures in the field.

In the presurgical evaluation of patients with drug-resistant focal epilepsy, the importance of detecting and delineating MRI lesion is of critical importance. Discovering a previously undetected lesion can dramatically change the subsequent approach and finally improve surgical outcome. The absence of a lesion on MRI has consistently been shown as a predictor for surgical failure (Bien 2009, Jeha 2007). On the other hand, MRI-lesional (MRI-positive) surgical candidates have demonstrated seizure-free outcome more than twice as high as MRI-nonlesional (MRI-negative) patients (Tellez-Zenteno et al. 2010). Guidelines or consensus recommendations on imaging standards in epilepsy further increase efficiency and improve high standard of care within the network. The aim was to exchange best practice and promote

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harmonisation of imaging standards for rare and complex epilepsies translated into a patient care pathway.

An objective was to set neuroimaging recommendations to improve the identification of etiology in patients with rare and complex epilepsies and mainly to improve detection of subtle lesions in MRI or to identify epileptogenic network by the means of functional neuroimaging in patients undergoing the presurgical evaluation and finally improve their surgical outcome. Another objective was to create a database of neuroimaging findings in the specific rare and complex epilepsies and of healthy control images with further research implications. The register of patients with specific epilepsy syndromes or etiologies (e.g. neurometabolic syndromes, genetic syndromes, inflammatory epilepsies) may serve to enable the collection and review of images to characterize imaging findings and for pattern recognition, both for scientific and clinical purposes. In order to enable the development and use of a centralized web-based imaging post-processing tool for presurgical evaluation, we need a large collection of healthy volunteer brain MRI's, from different scanners, field strengths, and ages.

2. Activities carried out and results

Update on network members' imaging standards and implementation of recommendations has been obtained through structured survey – results available at the EpiCARE webpage. In summary, survey in the year 2017 on use of imaging has been responded by 26 EpiCARE centers out of 28 (response rate 93%). In that time, 20 centers (77%) used 3T for their standard MRI epilepsy protocol in children, 22 (90%) centers in adults. For presurgical evaluation 3T was available in all centers for adults, and in 21/26 (81%) centers for children. MRI protocols of most of the centers 18 (82%) in adults, and 17 (71%) in children, met in that time recommended criteria for slice orientation and thickness for each of the sequences (3D volume T1 isotropic resolution $\leq 1\text{mm}$ and axial T2, coronal T2, axial FLAIR and coronal FLAIR each with slice thickness $\leq 3\text{mm}$) (Wellmer et al., 2013). 50% of all centers performed all MRI sequences with slice orientation as recommended in the guidelines. 17/26 centers (65%) performed some sort of MRI morphometric analysis for post-processing purposes

Since the survey in 2017 the new recommendation for the use of structural imaging has been published by the International League Against Epilepsy Neuroimaging Task Force (Bernasconi et al. 2019) and is available at the ILAE webpage <https://www.ilae.org/guidelines/guidelines-and-reports>. The protocol with substantial changes in comparison to previous recommendation should have been adopted by all the EpiCARE centres. A new survey is currently circulated to ensure how centres are able to adhere to the new protocol. As imaging protocols present a moving target there will be a need for the network to monitor this issue on regular basis to ensure high standard of care within the network.

Protocols for specific patient groups (e.g. TSC or neonates) have been discussed within the group and there was agreement that the new protocol (Bernasconi et al. 2019) is covering sufficiently for most of these specific groups as well. Based on the results of current survey expert-opinion/consensus recommendations for imaging in specific epilepsy subtypes and populations will be achieved if deemed necessary.

Systematic reviews on the use of neuroimaging methods have been published (Rados et al., 2021) and available at the EpiCARE webpage or are ready for submission for publication.

Development of a secure neuroimaging database for patients and controls has been discussed within the group several times with a focus on technical and legal aspects. A survey was circulated to the EpiCARE centres. Eleven sites ERN sites reported that they kept a database of healthy adults and eight were open to possibility to share their data. A multidisciplinary meeting was organized to discuss legal ramification and GDPR compliance of this step. Other option explored was a decentralized database of neuroimaging data where only metadata were stored on centralized storage and physical data were archived on local servers of cooperating centre. This option was assessed as a less preferable as it introduced more points of security failure and data breach, however this solution would have ensured maximum data control for cooperating sites. A close cooperation with Human Brain Project was also discussed using their Medical Informatic Platform which is able to perform federated analysis of data distributed across several hospitals, without moving data out, or uploading or copying these data. In addition, federated analyses are performed on fully anonymized data, and only provide aggregated results (no individual findings available).

Finally, the decision was adopted to create a database of control neuroimaging data that would be used for post-processing tool under ERN IT platform. IT department of ERN has been approached to provide us with the support, i.e. to create web-based database of anonymized control data in nifti or dicom with individualized access for all centres of EpiCARE. Centres should have been able to securely upload the anonymized data with custom labels (sex M/F, age, sequence, field strength). The database should have allowed for (mass) download of data according to defined labels. To run the database for the patient's data there was a need to add identification code of the centre/patient and diagnosis code to the custom label. The viewer (same as in CPMS) should be available to review the patient's data. If data were to be downloaded the centre providing the data had to give the permission. All accesses should have been logged. Informed consent of patients would be uploaded by the centre providing the data. Unfortunately, the IT department of ERN has not been able to support this plan

5 Conclusions

The recommendation for the use of structural imaging has been published by the International League Against Epilepsy Neuroimaging Task Force (Bernasconi et al. 2019) and is available at the webpage <https://www.ilae.org/guidelines/guidelines-and-reports>. The protocol should be used by all the EpiCARE centres and a survey is currently circulated to ensure that all the centres have already adopted a new protocol or to identify if there are some specific technical, logistical or personal barriers. Recent systematic reviews on imaging are available at the EpiCARE website. Development of secure neuroimaging database for patients and controls has been temporarily abandoned.

The results achieved are in accordance with most of the objectives for Work Package, as detailed above.

6 Bibliography / References

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