Title page: Routine and sleep EEG: minimum recording standards of the International Federation of Clinical Neurophysiology and the International League Against Epilepsy

#### Authors:

Maria E Peltola<sup>1</sup>, Markus Leitinger<sup>2</sup>, Jonathan J Halford<sup>3</sup>, Kollencheri Puthenveettil Vinayan<sup>4</sup>, Katsuhiro Kobayashi<sup>5</sup>, Ronit M Pressler<sup>6</sup>, Ioana Mindruta<sup>7</sup>, Luis Carlos Mayor<sup>8</sup>, Leena Lauronen<sup>1</sup>, Sándor Beniczky<sup>9</sup>

Author affiliations:

<sup>1</sup>HUS Diagnostic Center, Clinical Neurophysiology, Clinical Neurosciences, Epilepsia Helsinki, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

<sup>2</sup>Department of Neurology, Christian Doppler University Hospital, Paracelsus Medical University Salzburg, Austria

<sup>3</sup>Department of Neurology, Medical University of South Carolina, Charleston, SC, USA

<sup>4</sup>Department of Pediatric Neurology, Amrita Institute of Medical Sciences, Cochin, Kerala, India

<sup>5</sup>Department of Child Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

<sup>6</sup> Clinical Neuroscience, UCL- Great Ormond Street Institute of Child Health and Department of Clinical Neurophysiology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

<sup>7</sup>Department of Neurology, University Emergency Hospital of Bucharest and University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

Department of Neurology, Hospital Universitario Fundacion Santa Fe de Bogota, Colombia

<sup>9</sup>Department of Clinical Neurophysiology, Aarhus University Hospital, Aarhus, and Danish Epilepsy Centre, Dianalund, Denmark

Corresponding author: MD, PhD Maria Peltola, Stenbäckinkatu 9, PL290, 00029 Helsinki, Finland; email: maria.peltola@hus.fi, ORCID 0000-0001-8336-0586

Co-authors' email addresses:

Markus Leitinger: ma.leitinger@salk.at

Jonathan J Halford: <a href="mailto:halfordj@musc.edu">halfordj@musc.edu</a>

Kollencheri Puthenveettil Vinayan: <a href="mailto:drvinayan@gmail.com">drvinayan@gmail.com</a>

Katsuhiro Kobayashi: k koba@md.okayama-u.ac.jp

Ronit M Pressler: <u>ronit.pressler@gosh.nhs.uk</u>

Ioana Mindruta: ioanamindruta@me.com

Luis Carlos Mayor: <u>Luis.Mayor@fsfb.org.co</u>

Leena Lauronen: <u>leena.lauronen@hus.fi</u>

Sándor Beniczky: <a href="mailto:sbz@filadelfia.dk">sbz@filadelfia.dk</a>, ORCID 0000-0002-6035-6581

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provocations

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Sándor Beniczky has served as scientific consultant for Epihunter and received speaker honoraria from

Natus. Jonathan J. Halford has served as a Board Advisor for CortiCare. Ronit M Pressler is an

investigator for studies with UCB and does consultancy work for Kephala, Ireland. She served as a

speaker and/or on Advisory Boards for Natus, GW Pharmacceuticals, Esai, and UCB. The remaining

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**Ethical Publication Statement** 

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm

that this report is consistent with those guidelines.

# Routine and sleep EEG: minimum recording standards of the International Federation of Clinical Neurophysiology and the International League Against Epilepsy

Maria E Peltola<sup>1</sup>, Markus Leitinger<sup>2</sup>, Jonathan J Halford<sup>3</sup>, Kollencheri Puthenveettil Vinayan<sup>4</sup>, Katsuhiro Kobayashi<sup>5</sup>, Ronit M Pressler<sup>6</sup>, Ioana Mindruta<sup>7</sup>, Luis Carlos Mayor<sup>8</sup>, Leena Lauronen<sup>1</sup>, Sándor Beniczky<sup>9</sup>

<sup>1</sup>HUS Diagnostic Center, Clinical Neurophysiology, Clinical Neurosciences, Epilepsia Helsinki, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

<sup>2</sup>Department of Neurology, Christian Doppler University Hospital, Paracelsus Medical University Salzburg, Austria

<sup>3</sup>Department of Neurology, Medical University of South Carolina, Charleston, SC, USA

<sup>4</sup>Department of Pediatric Neurology, Amrita Institute of Medical Sciences, Cochin, Kerala, India

<sup>5</sup>Department of Child Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

<sup>6</sup> Clinical Neuroscience, UCL- Great Ormond Street Institute of Child Health and Department of Clinical Neurophysiology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

<sup>7</sup>Department of Neurology, University Emergency Hospital of Bucharest and University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

<sup>8</sup>Department of Neurology, Hospital Universitario Fundacion Santa Fe de Bogota, Colombia

<sup>9</sup>Department of Clinical Neurophysiology, Aarhus University Hospital, Aarhus, and Danish Epilepsy Centre, Dianalund, Denmark

Corresponding author: MD, PhD Maria Peltola, Stenbäckinkatu 9, PL290, 00029 Helsinki, Finland; email: maria.peltola@hus.fi

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#### Summary

This paper provides recommendations on minimum standards for recording routine ("standard") and sleep electroencephalography (EEG). The joint working group of the International Federation of Clinical Neurophysiology (IFCN) and the International League Against Epilepsy (ILAE) developed the standards according to the methodology suggested for epilepsy-related clinical practice guidelines by the Epilepsy Guidelines Working Group. We reviewed the published evidence using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement. The quality of evidence for sleep induction methods was assessed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) method. A quality assessment tool for diagnostic accuracy studies (QUADAS-2) was used to assess risk of bias in technical and methodological studies. Where high quality published evidence was lacking, we used modified Delphi technique to reach expert consensus. The GRADE system was used to formulate the recommendations. The quality of evidence was low or moderate. We formulated 16 consensus-based recommendations for minimum standards for recording routine and sleep EEG. The recommendations comprise the following aspects: indications, technical standards, recording duration, sleep induction and provocative methods.

### Key points

- Minimum standards are needed to improve accuracy, efficacy and reliability of recording routine and sleep electroencephalography (EEG).
- 2. The overall quality of research evidence was low leading to conditional recommendations, based on consensus.
- We formulated 16 recommendations for minimum standards for recording routine and sleep EEG.
- 4. Implementation strategies need to be tailored by local organizations or chapters.

#### 1 Introduction

Non-invasive electroencephalography (EEG) remains an essential non-invasive method for analyzing electrophysiological brain activity in epilepsy and in selected disorders of brain dysfunction<sup>1,2</sup>. Although, practical definition of epilepsy is clinical<sup>3</sup>, scalp EEG has an important role not only in the diagnosis of epilepsy, but also in the follow-up if the disease evolves, and in the classification of the epilepsy syndromes<sup>2,4,5</sup>.

The International League Against Epilepsy (ILAE) Neurophysiology Task Force has recently addressed the use of EEG as a clinical tool in the classification of the epilepsy syndromes<sup>4,5</sup>. Regarding the variable resources of EEG service worldwide, they distinguished two levels of EEG recording, basic and advanced. Routine EEG with activation procedures corresponds to the basic level and sleep induction is used at the advanced recording level. Epileptiform discharges are modulated by sleep and show higher frequency in non-rapid eye movement (NREM) sleep than awake<sup>6-8</sup>. Most clinical studies suggest an added diagnostic value of sleep EEG compared to standard EEG<sup>9-12</sup>, yet a few studies question the utility of sleep EEG<sup>13,14</sup>. The sensitivity of EEG for epileptiform discharges increases with repeated recordings<sup>15</sup> and if one repeats the EEG, it is recommended to do a sleep EEG in the second round. In some patients (especially children), the routine wake recording can be so obscured by artifact such that little undisturbed background is visible, in which case a sleep EEG is recommended.

Establishing and maintaining technical standards aim at ensuring the high quality of laboratory investigations. The minimum standards represent a set of recommendations that can be readily adapted by countries and applied to laboratories at any level of the health-care system<sup>16</sup>.

In 2002 the Commission on European Affairs of the ILAE has published recommendations for recording EEG across Europe<sup>17</sup>, but this has not been updated since. A survey organized in 2017 within 28 members of the European Reference Network for rare and complex epilepsies (ERN EpiCARE) showed that almost all centers used local guidelines to record EEG<sup>18</sup>. In addition, a lack of common standards for recording routine EEG impedes high quality multicenter research projects as was observed in the recently completed Human Epilepsy Project 1 (unpublished data).

Several societies including the American Society of Clinical Neurophysiology, Canadian Society of Clinical Neurophysiology, French Society of Clinical Neurophysiology and the French League Against Epilepsy have recently published updated national recommendations for EEG recording standards<sup>19–21</sup>. The lack of minimum standards for recording EEG that are based on systematic review and unite work of international experts impedes the development of global standards for good clinical practices<sup>22</sup>.

The International Federation of Clinical Neurophysiology (IFCN) and the ILAE identified the need for a joint working group to define the minimum recording standards of EEG according to these standards.

The ILAE Guidelines Task Force approved the Working Protocol that was based on the methodology recommended by the ILAE for developing a Clinical Practice Guideline<sup>23</sup>. The protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement as applicable (Appendix 1).

The objective of this joint ILAE-IFCN paper is to provide recommendations on minimum standards for recording routine and sleep EEG. Target audience of the guideline is healthcare personnel referring patients to EEG, being responsible for EEG recordings, performing, analyzing, and reporting EEG.

#### 2 Methods

#### 2.1 Establishing a working group

The IFCN and the ILAE each appointed members to the joint working group. The IFCN-ILAE Working Group was composed of ten experts who were adult and pediatric neurologists with subspecialty in epileptology and clinical neurophysiologists. Members represented four of six regions of the World Health Organization (WHO). The IFCN-ILAE Working Group has been approved by the ILAE Guidelines Task Force.

#### 2.2 Developing clinical questions

To achieve the overall objective, the IFCN-ILAE Working Group defined five questions that were examined by five subgroups each containing 2-3 working group members (Table 1). Patient/population, Intervention, Comparison and Outcome (PICO) statements were used to organize the clinical questions when applicable.

#### 2.3 Search strategy

The literature search was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. We performed electronic search of PubMed and Embase databases for English literature between 1990 and September-December 2019. The full search strategies for PubMed and dates when last accessed the database are presented in Appendix 2.

#### 2.4 Study selection, data extraction and synthesis of results

Specific inclusion criteria were defined for each of five clinical questions. Studies on neonatal EEG, emergency EEG, intensive care monitoring, and long-term epilepsy monitoring were excluded, as they were beyond the scope of this guideline. We included:

1. Studies that addressed the utility of non-emergent EEG in diagnostics or follow up of patients; randomized control trials were searched for, but also studies evaluating the usefulness of EEG if a proper control group (no EEG) and follow up measures (impact on the patient care) were used.

- 2. Studies that addressed recording electrode array and montages, electrode impedance, synchronized video, sampling rate and frequency band, ancillary equipment, display settings, data storage and EEG data format.
- 3. Studies that compared yield of different length of EEG recordings and used the presence of EEG abnormalities as a primary outcome measure, and cost-benefit as a secondary outcome.
- 4. Studies that compared EEG recordings with sleep deprivation (either 24h or partial), studies with no sleep deprivation, studies that compared sleep deprivation to pharmacological sleep induction and studies that compared EEGs with different pharmacological sleep inductions, and studies with yield of sleep as outcome. Secondary outcomes included adverse effects and cost-benefit ratio of sleep induction.
- 5. Studies that addressed the utility of activations other than sleep and had the yield of epileptiform abnormalities, epileptic seizures, and psychogenic non-epileptic seizures as outcomes. Secondary outcomes included adverse effects.

At least two members of the subgroups independently reviewed the titles and abstracts to identify potentially eligible research articles. References of selected articles were screened for potentially eligible studies. Full text articles were reviewed by two independent reviewers for inclusion. Data extraction was designed independently for each clinical question.

#### 2.5 Quality rating of individual studies and synthesis of results

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method to assess the risk of bias of individual sleep induction studies that were pharmacological and non-pharmacological intervention studies<sup>23,24</sup> (Tables S11-S13). In other (non-interventional) studies, risk of bias was assessed by using a quality assessment tool for diagnostic accuracy studies (QUADAS-2) tool developed for primary diagnostic accuracy studies that better targeted potential study limitations involved in technical and methodological EEG studies, although not being diagnostic accuracy studies<sup>25</sup>

(Tables S9-S10, S14-S15). The risk of bias assessment was carried out by two reviewers that solved possible disagreements by discussion.

In addition, we classified studies as meta-analysis, systematic reviews, randomized controlled trials (RCT), observational studies including diagnostic accuracy studies, case series and guidelines.

Observational studies were further categorized, using predefined criteria to evaluate the evidence reflecting risk of bias given the paucity of high-level evidence<sup>2,26</sup>. Category I observational studies included large (N>50) prospective broad-spectrum studies and large blinded technical studies with an acceptable gold standard. Category II studies were large prospective narrow-spectrum studies, large retrospective broad-spectrum studies and small (N=10 – 50) blinded technical studies with an acceptable gold standard. Category III studies were large retrospective narrow-spectrum studies, small prospective and retrospective studies or technical studies that were not blinded or without an acceptable reference standard. Category IV were mathematical simulation studies.

Due to large heterogeneity of the studies, meta-analysis was not possible to conduct, and our synthesis was qualitative.

#### 2.6 Methods of recommendation

We assessed the overall quality of evidence for methods of sleep induction and yield of sleep during EEG recording using the GRADE approach (Table S13) and for outcomes of other clinical questions by the risk of bias and classification and category of individual studies (Tables S1-S2, S7-S10, S14-S15). Due to low overall quality of evidence, a modified Delphi process was used to formulate recommendations by each subgroup<sup>27</sup>. The modified Delphi process consisted of a series of written questionnaires that were answered anonymously (Appendix 3), followed by open consensus discussions concerning each clinical question. The iteration was continued until agreement of at least 2/3 of the IFCN-ILAE Working Group members was achieved. One member of each subgroup designed the Delphi questions, provided supportive analysis of literature, did not answer to written questions but analyzed results and chaired

the consensus discussion that was organized as a web-meeting. The strength of the recommendation was rated following the ILAE guideline of developing clinical practice guidelines<sup>23</sup>.

#### 3 Results

#### 3.1 Indications of routine and sleep EEG

We found 121 articles through database search and six additional articles from other sources. After removing the duplicates, 99 articles remained for screening of abstracts. Fourteen full-text articles were assessed for eligibility. Three guidelines were included. None of the 11 research studies met the eligibility criteria. The reason for exclusion was lack of proper study design and methodology to study the indications for routine and sleep EEG. Screened studies described EEG finding on specific illnesses showing indirect evidence of utility of EEG. However, expanding the systematic review to include specific diseases in search terms, would have rendered the work exhaustive and less objective. PRISMA chart is included in Appendix 4A.

Previous consensus-based guidelines on the best practice of recording and reporting of EEG in adults and children include the general indications for EEG<sup>1,17,21</sup>. They all emphasized that 'clinical suspicion of epilepsy' was the main indication for EEGs. Recently published clinical summaries determine the value of EEG for the diagnosis of seizures and epilepsy and monitoring of epilepsy<sup>2,4,5,28</sup>. They discuss the sensitivity and specificity of interictal epileptiform discharges, the value of routine and sleep EEG in the diagnosis and classification of the epilepsy type and the role of EEG in making decisions regarding antiseizure medication withdrawal.

#### 3.1.1 Recommendation

We conclude that the quality of evidence on indications of routine and sleep EEG is very low. Through a modified Delphi technique, we reached a consensus on the indications of routine and sleep EEG that

justifies a weak (conditional) recommendation on the indications of EEG recorded by appointment in non-emergent situation (Table 2).

#### 3.2 Technical standards

Eighteen articles were found in the search and 14 additional articles were identified through other sources. After removal of duplicates, 30 abstracts were screened for eligibility and ten full-text articles were included in the qualitative synthesis. PRISMA chart is included in Appendix 4B. Four of the articles were guidelines<sup>17,21,29,30</sup> and six were Category III observational studies<sup>31–36</sup> (Table S1). Individual studies had low risk of bias (Table S9). However, low observational study category and heterogeneity (variable outcomes) downgraded the quality of evidence. In the previous guidelines of recording EEG<sup>17,21,29</sup>, technical standards were based on expert opinion without systematic review or quality rating of scientific studies.

We conclude that the quality of evidence on technical EEG standards is low. Our recommendation is conditional and formulated by consensus of modified Delphi discussions. Table 3 summarizes the conditional recommendation for technical standards. Skin safety was beyond the scope of our paper, but we refer the reader to the previously published recommendations<sup>37,38</sup>.

#### 3.2.1 Electrodes and montages

For routine EEG, the use of either gold or silver/silver-chloride cup electrodes individually applied with electrode paste or gel are suggested. Head caps are becoming more commonly used and are also acceptable if electrode impedances are checked and meet standards. Dry electrode EEG systems are not recommended yet, because they are associated with increased movement and sweat artifacts and the effectiveness of methods for mitigating this, such as automated artifact removal, have yet to be thoroughly studied<sup>34</sup>. MRI compatible electrodes and needle electrodes are acceptable in certain circumstances. The use of the 25 electrode IFCN montage, which adds six additional subtemporal

electrodes to the 10-20 array and uses 10-10 electrode nomenclature<sup>30</sup>, is suggested to be used whenever feasible, because there is evidence that it improves the ability to detect both ictal<sup>32</sup> and interictal<sup>39–41</sup> epileptiform discharges. Otherwise the 10-20 array is acceptable<sup>30,32,33,35</sup>.

One electrocardiography (ECG) channel should be used. It is also suggested to record at least two electromyography (EMG) channels if motor events of clinical interest are suspected. Two EMG channels (if electrodes are placed on extremities bilaterally) provide an objective measurement of body movement which can be correlated to the EEG and can help in the identification of elementary motor seizure semiology (myoclonus, spasms, clonic, tonic, tonic-clonic seizures) and in the differentiation between tonic and atonic seizures <sup>42–45</sup>.

Routine recording of the time-synchronized video to document seizure manifestations and possible sources of artifacts with at least one camera is strongly suggested. Video is essential in all patients with suspected epilepsy or clinical events.

Two electrooculogram (EOG) leads may be placed in cases in which it is difficult to distinguish eye movement artifacts from slow EEG waves, and these leads should be placed according to the recommendations of the IFCN<sup>30</sup> and the American Academy of Sleep Medicine<sup>46</sup> - 1 cm lateral and above the outer canthus on the right and one cm lateral and below the outer canthus on the left.

#### 3.2.2 Electrode impedances

In addition to visual signal quality control, it is advisable to check scalp-electrode impedance at the beginning of each EEG recording. Impedances below 100  $\Omega$  are unacceptable, as it often indicates shunting through a salt bridge on the scalp. In order to reduce the impact of disturbances and obtain a scalp-electrode impedance lower than 5 k $\Omega$ , skin abrasion is still required, but in a small subset of cases it is not proposed<sup>31</sup>. There is some evidence that a scalp-electrode impedance of 10 k $\Omega$  or higher is acceptable because modern EEG amplifiers have a relatively high input impedance<sup>31,36</sup>. These studies

have only measured EEG signal amplitude, amplitude of 60 Hz artifact, and ability to resolve evoked potentials between electrodes with varying impedances. Studies of EEG signal quality as perceived by experts in electrodes of varying impedances are lacking. Electrodes with higher impedance can be more affected by sweat, movement, and electrode pop artifact. Additionally, allowing impedance values up to  $10~\mathrm{k}\Omega$  increases the chance that there will be a significant imbalance among the impedances of the array of electrodes. Unbalanced impedances can compromise the ability of an EEG amplifier to reject potentials that are the same at a pair of electrodes while amplifying those that are different (common mode rejection). Therefore, impedance values below  $5~\mathrm{k}\Omega$  are suggested and an impedance value of less than  $10~\mathrm{k}\Omega$  is considered acceptable.

#### 3.2.3 Recording and review settings

For routine EEG in current clinical practice, frequencies of over 100 Hz are not currently considered of clinical interest. This may change in the future, with the increased use of commercial artifact reduction systems using blind signal source separation, which may work better if given EEG signals with higher signal frequency content. The Nyquist theorem specifies that the highest measurable frequency is half the sampling rate. For example, with a 256 Hz sampling rate, the highest frequency that can be resolved is 128 Hz. In actuality, because of phase alignment, it is necessary to discretely sample (digitize) the signal at a rate of at least 2.5 times the highest frequency component of the signal<sup>47</sup>. Therefore, based on the experience of experts and the frequency content of clinically relevant EEG signals, the proposed minimum sampling rate is 256 Hz.

For visualization (display), the suggested low-pass (high frequency) filter setting is 70 Hz, and the suggested high-pass (low frequency) filter setting is 0.5 Hz. A value of 7  $\mu$ V/mm is the proposed display resolution, except for children's recordings in which 10  $\mu$ V/mm is suggested. It is recommended that EEG reviewers be allowed to change the gain of channels independently, adjust time resolution, display

voltage maps at a time point, add and change annotations during review, apply notch filters and adjust low-pass and high-pass filters if needed.

#### 3.2.4 Data storage and export

We suggest archiving the entire EEG recording as well as the time-synchronized video either for the entire recording or video only from clinically relevant events, preferably with a backup copy. Good data security policy needs to be ensured. It is recommended that users be able to export EEG data for research in Comma Separated Values (CSV) or European Data Format (EDF). The International Federation of Clinical Neurophysiology is working with Digital Communication in Medicine (DICOM) to create a modern format for storage and exchange of EEG data, which will become available within the next few years<sup>48</sup>.

#### 3.3 Duration of recording

The database searches generated 156 articles and 19 additional articles were identified from other sources. After removing duplicates, 152 abstracts were screened. Forty-one of full text articles were assessed for eligibility. Twelve articles, three of them EEG recording guidelines, were included in qualitative analysis. PRISMA chart is included in Appendix 4C.

We identified nine eligible original research papers, two of them category I<sup>49,50</sup> and seven category II-III<sup>51–57</sup> observational studies. Study characteristics are summarized in Table S2. Only two Category II studies evaluated the optimal duration of sleep EEG<sup>51,54</sup>. All studies included QUADAS-2 domains with high risk of bias (Table S10). Most studies were at high risk of biased reference standard.

The previous consensus-based guidelines of ILAE (Commission Report Commission on European Affairs: Subcommission on European Guidelines), American Clinical Neurophysiology Society and Canadian Society of Clinical Neurophysiologists recommend of at least 20 minutes technically satisfactory recording for routine EEG<sup>17,21,29</sup> and 30 minutes for sleep EEG<sup>21</sup>.

A category I study in children and adults found that the sensitivity of the 15 min routine EEG compared with the 25 minute-EEG for epileptiform or non-epileptiform abnormality, was 94.1% [CI:88.7-97.4%], and the specificity 99.3% [CI:97.5 -99.9%]<sup>49</sup>. The sensitivity of 15 minute-EEG increased when only epileptiform abnormalities were considered (97.1% [CI: 92.6-99.2%]). Authors estimated 15-minute routine EEG to be cost effective, but recording procedure had to be rigorous to include activations, too. In agreement, a category II study in children found that reducing the recording time of routine EEG from 20 to 15 minutes may miss epileptiform abnormalities in 2.36% [CI: 0.63–4.09%] of EEGs<sup>52</sup>. The largest category II retrospective study conducted in a tertiary epilepsy center found significant decrease in the diagnostic yield for recordings shorter than 20 minutes<sup>54</sup>. They did not find significant difference between the yield of 20 and 30-minute routine EEG or between the yield of 30 and 60-minute sleep EEG in adult patients.

In a category I study in children and adults, interictal epileptiform abnormalities became only apparent after the initial 30 minutes in 4.5% of patients (81/1803) <sup>50</sup>. The relative increase in yield of interictal epileptiform abnormalities was 19.1% [CI: 15.6–23%]. Also, in a category II study the yield of epileptiform abnormalities was increased by 11% (p=0.001) by lengthening the recording from standard 20 to 40 minutes<sup>55</sup>. A category II study observed 51% of epileptiform abnormalities within 20 minutes of sleep-deprived EEG, 71% within 30 minutes and 93% within 90 minutes<sup>51</sup>.

#### 3.3.1 Recommendation

The quality of evidence on optimal duration of routine and sleep EEG is low. Therefore, our recommendations are conditional. Consensus after modified Delphi discussions is to suggest the duration of 20 minutes for the routine EEG and 30 minutes for the sleep EEG excluding preparation (Table 3).

It is advisable to book the sleep recording of infants and children in the postprandial period, where there is a higher chance to fall asleep. Based on clinical expertise, we propose individualizing the

recording time and duration when improved yield is expected<sup>4,5</sup>. Booking morning time for patients with suspected juvenile myoclonic epilepsy, prioritizing sleep recording in patients with suspected or diagnosed self-limited focal epilepsy of childhood or infantile epileptic spasms syndrome, and on suspicion of infantile epileptic spasms syndrome, extending recording at least 10 minutes after awakening to increase the probability of recording of epileptic spasms probably increase the yield of EEG.

#### 3.4 Sleep inducing methods

The database searches generated 360 articles and 20 additional articles were identified from other sources. After removing duplicates, 259 records were screened. Sixty-nine full text articles were assessed for eligibility. Seventeen studies fulfilled the eligibility criteria and three of them were guidelines. PRISMA chart is shown in Appendix 4D.

All except one study evaluated the efficacy of sleep induction in children and young adults up to age of 18 years<sup>58</sup>. The previous EEG recording guidelines<sup>17,21,29</sup> do not recommend particular sleep inducing method in adults, but recommend natural sleep in children<sup>17,21</sup> and if it fails, partial sleep deprivation or melatonin<sup>21</sup>.

One RCT with indirectness and three category II observational studies without serious study limitations compared the yield of sleep in EEGs with partial sleep deprivation to EEGs without sleep deprivation in children and young adults (Tables S3, S11-S13). The studies did not represent all WHO regions. Burden of sleep deprivation to patient, family and society is very likely to be culturally biased. None of the studies used a stressful 24h sleep deprivation. Ten studies including six RCTs with high risk of bias and four observational studies with high risk of bias explored the sleep-inducing efficacy of melatonin or another drug (Tables S4-S6, S11-S13). The studies showed inconsistency and imprecision because of heterogeneous methods, small number of studies and small sample size in many studies. Publication bias was considered possible for 24h sleep deprivation and use of sedative drugs other than melatonin

that have been used more commonly before 1990 but have been abandoned because of adverse effects.

Data on adverse effects of sleep-inducing methods was assessed in nine studies using sleep-inducing drugs (Tables S4-S6). However, study limitations were serious (Tables S11-S12).

#### 3.4.1 Efficacy of sleep induction

Partial sleep deprivation was shown to increase the probability of obtaining sleep during EEG<sup>9,13,14,59</sup> (Table S3).

A category I and a category II study showed that melatonin and partial sleep deprivation are equally efficacious in inducing sleep<sup>60,61</sup>. A category II study suggested that melatonin may be more efficacious in younger children aged 1-4 years in comparison to older children<sup>61</sup>.

A category I multicenter study found combined intervention of sleep deprivation and melatonin to be significantly more effective to induce sleep than either method alone in pediatric patients<sup>62</sup>. However, a smaller category I study did find improved yield of sleep when melatonin was combined with partial sleep deprivation<sup>63</sup>.

In a category I study<sup>60</sup>, sleep latency was significantly shorter with melatonin (mean latency 21 min) compared to partial sleep deprivation (mean latency 34 min), but the result was not confirmed by another category I study<sup>63</sup>. Sleep latency was also significantly reduced by combining melatonin with partial sleep deprivation in comparison to melatonin and partial sleep deprivation alone in a category I study<sup>62</sup>.

There was no difference in the yield of epileptiform abnormalities between the intervention groups in any of the included studies.

Significant adverse effects of melatonin were not found in category I observational studies and randomized controlled trials that systematically assessed them in pediatric patients<sup>58,60,63,66</sup>.

Disadvantages of sleep deprivation included difficulties to keep children awake at night and to wake up in the morning in 50% of patients<sup>60</sup>. In two studies, generalized tonic-clonic seizures occurred coincidentally with sleep deprivation in one patient<sup>9,59</sup>.

We also collected data on melatonin dose used in the studies which varied from 2 mg to 10 mg. There are no trials on dose dependency for acute hypnotic or anxiolytic use of melatonin in children. In young healthy adults, increasing the dose from 1.0 to 10 mg did not significantly reduce the sleep-onset latency or the subjective sleepiness<sup>64</sup>. Clinical consensus recommendation by a group of European pediatric neurologists suggests a dose of 1-3 mg 30 min before the examination<sup>65</sup>.

There is no evidence of advantage of use of other sleep-inducing drugs than melatonin when potential benefits and adverse effects are outweighed (Tables S5-6)<sup>58,66-70</sup>.

#### 3.4.2 Recommendation

We conclude that the quality of evidence on efficacy of partial sleep deprivation to induce sleep during EEG recording is moderate in children and young adults. However, it is very low for pharmacological sleep-inducing methods due to study limitations, imprecision caused by small number of studies and small sample sizes, and adverse effects. We suggest partial sleep deprivation as a primary sleep-inducing method in adults and children 12 years of age or older who can cooperate to the sleep deprivation (Table 3). Sleep deprivation is a feasible method regardless of availability of drugs and personnel needed for administration of drugs. An example of suggested partial sleep deprivation protocol is shown in Table 4. However, it is important to note that there are no studies evaluating the safety of partial or full sleep deprivation for any age group. Sleep deprivation may also cause significant distress to a child and family.

Melatonin or sleep deprivation are suggested as a primary sleep induction method in children under 12 years of age (Table 3). If sleep deprivation or melatonin fails to induce sleep, the combination of both methods may be more effective. We also suggest melatonin as a primary sleep induction method in children and adults who cannot cooperate to partial sleep deprivation. The proposed dose of melatonin is 1-3 mg administered 30-60 min before the start of the EEG recording. If melatonin is not available in the market, chloral hydrate may be used when partial sleep deprivation fails to attain sleep and patient safety is ensured.

#### 3.5 Provocative methods

The database searches generated 3483 records and 13 articles were identified from other sources. After removing duplicates, 3049 abstracts were screened. One hundred twenty-eight full-text articles were examined for eligibility. Forty-two original research studies and four guidelines<sup>17,21,29,71</sup> were included for review. PRISMA chart is shown in Appendix 4E. Eighteen observational studies evaluated the use of hyperventilation (Table S7), 24 intermittent photic stimulation (IPS) (Table S8) and nine studies<sup>72–80</sup> compared other provocation methods with IPS, hyperventilation and/or sleep. A part of the studies investigated several provocation methods. All studies were at high risk of bias because of limitations in both index and reference tests (Tables S14 and S15).

#### 3.5.1 Hyperventilation

#### 3.5.1.1 Protocol and technical standards

We found only two studies assessing hyperventilation protocol<sup>81,82</sup>. In a category I study, 16% of seizures, 30.4% of interictal EEG abnormalities, and 30% of epileptiform discharges provoked by hyperventilation occurred during the last 2 min of the 5 min hyperventilation<sup>81</sup>. On the other hand, 85.5% of absence seizures were elicited within 1.5 min of hyperventilation in a category III study<sup>82</sup>. Earlier EEG guidelines recommend minimum of three minutes of hyperventilation that should be prolonged or repeated in a strong suspicion of typical absence seizures<sup>17,21,29</sup>.

#### 3.5.1.2 Yield of hyperventilation

We found three large category I studies that showed an additional diagnostic value of hyperventilation<sup>81,83,84</sup>. Hyperventilation precipitated epileptiform abnormalities that were not present in a baseline EEG in 0.92% (3/326)<sup>83</sup>, 1.1% (10/877)<sup>81</sup> or 3.0% (95/3170)<sup>84</sup> of adult and pediatric patients. These results were supported by two Category II studies reporting epileptiform abnormalities only during hyperventilation in 0.86% (5/580)<sup>85</sup> and 5.7% (8/141) of patients<sup>86</sup>. In a category III study in patients with newly diagnosed epilepsy, hyperventilation provoked epileptiform abnormalities not present in baseline in 7.7% (25/325) of patients<sup>87</sup>. The yield was greatest for patients 1-19 years old (10.3%). In a study including EEGs of 100 healthy young men, no epileptiform activity was elicited by hyperventilation<sup>88</sup>.

Significant increase in frequency of epileptiform discharges compared with baseline was found in 23.7% (14/59) of patients with genetic generalized epilepsy in a category III study<sup>75</sup>.

#### 3.5.1.3 *Safety*

In a category I study assessing safety of hyperventilation, no significant cerebrovascular, cardiovascular or respiratory events were observed<sup>84</sup>. Seizures during hyperventilation were relatively rare. Two category I studies reported seizures that were provoked by hyperventilation in 2.2% (69/3170) and exclusively by HV in 2.9% (25/877) of patients referred to EEG on suspicion of epilepsy<sup>81,84</sup>. Only 1/3170 patients had a generalized tonic clonic seizure<sup>84</sup>. In a random sample of 580 reports of routine EEG with HV of category II study, seizures provoked by hyperventilation were reported in 2.1% (12/580) of records<sup>85</sup>. Comparable or lower incidence of seizures during hyperventilation were reported in smaller category II and category III studies including narrow-spectrum studies on patients with genetic generalized epilepsy <sup>76,86,89</sup>.

Three category I studies observed psychogenic non-epileptic seizures in 1.1% (10/877) and 0.9% (31/3475) of patients<sup>81,84</sup>, and in none (0/326)<sup>83</sup> during hyperventilation. A category III showed increased

frequency of psychogenic non-epileptic seizures when patients were informed about a potential seizure inducing effect of hyperventilation<sup>90</sup>.

#### 3.5.2 Intermittent photic stimulation

#### 3.5.2.1 Protocol and technical standards

We identified only two category II<sup>91,92</sup> and one category III<sup>93</sup> studies assessing the intermittent photic stimulation (IPS) protocol. Out of 45 patients with a photoparoxysmal response, this was elicited only on eye closure during IPS in 24.4%<sup>91</sup>. Photoparoxysmal response occurred in 8.0% (21/263) of children, and 45% of responses were found after 9 seconds of stimulation which led to the recommendation for using 10 or more seconds for each stimulus frequency<sup>92</sup>. In photosensitive patients, the photosensitivity range for frequencies of 25-60 Hz was significantly higher (maximal) in the condition "eyes open with diffuser" compared with "eyes open", and "eyes closed", and "eye closure" (p=0.0002)<sup>93</sup>. Earlier EEG guidelines include the recommendation of a European expert panel on methodology of photic stimulation<sup>71</sup>.

#### 3.5.2.2 Yield of intermittent photic stimulation

We identified one category I study that provided evidence for an additional diagnostic value of IPS<sup>94</sup>. Intermittent photic stimulation revealed generalized epileptiform discharges that were not present in the EEG before stimulation in 1.5% (79/5383) of patients, and the only useful information (epileptiform discharges, epileptic or non-epileptic seizures) in 2.3% (122/5383) of patients<sup>94</sup>.

In line, in category II studies IPS elicited generalized epileptiform discharges (a type 4 photoparoxysmal reaction<sup>95</sup>) as only epileptiform activity in 0.68% (5/732) of EEGs<sup>85</sup> and epileptiform abnormalities occurring only on photic stimulation in 5.3% (12/226) of EEGs<sup>86</sup>. In comparison, 0.32% (44/13658) of Air Force applicants showed epileptiform abnormalities induced only on photic stimulation<sup>96</sup>. On the other hand, IPS provoked the only epileptiform abnormalities in 30.5% of patients with genetic (idiopathic) generalized epilepsy aged 14 - 17 years in a category III study<sup>75</sup>.

A category III study showed an additional yield of IPS in 3.7% (15/406) of patients with newly diagnosed epilepsy compared to baseline<sup>87</sup>. Repeated IPS in the second EEG after the first normal one, captured epileptiform activities in 3.0% (5/164) of patients. The yield was greatest for the patients under 20 years of age and for the patients with generalized seizures.

In a category II study, a photoparoxysmal response was found in 2.3% of 2,888 consecutive EEG recordings and in 10% of patients with epilepsy<sup>91</sup>.

A category III study found photoparoxysmal response type 1 to 4<sup>95</sup> ranging from focal occipital spikes to generalized spikes and waves in 74% of patients with epilepsy with generalized tonic clonic seizures on awakening, in 56% in juvenile absence epilepsy, in 50% in juvenile myoclonic epilepsy, and 44% in childhood absence epilepsy compared with 23% in childhood epilepsy with centro-temporal spikes and 16% in symptomatic/cryptogenic epilepsy<sup>97</sup>. The relative frequency of type 4 among all photosensitivity reactions was significantly higher in genetic generalized epilepsy (59%) than in childhood epilepsy with centro-temporal spikes (38%). In a nationwide study in Great Britain, annual incidence of patients with epilepsy and generalized spike-and-wave discharges on IPS on their first EEG was roughly 1.1 per 100,000, representing approximately 2% of all new cases of epilepsy<sup>98</sup>.

#### 3.5.2.3 *Safety*

In a nationwide UK category I study, 0.72% (39/5383) of patients had seizures due to IPS including a generalized tonic clonic seizure in 0.04% of patients<sup>94</sup>. In 0.9% (49/5383) of patients, the IPS provoked a psychogenic non-epileptic seizure<sup>94</sup>. In accordance, two category II studies reported seizures exclusively during IPS in 0.53% (1/189) and 0.68% (5/732) of patients<sup>85,86</sup>. The intermittent photic stimulation caused epileptic seizures in 0.068% (4/5,893) of Air Force applicants, of which three out of four were generalized tonic-clonic seizures<sup>99</sup>. In a category III study, the rate of psychogenic non-epileptic seizures rose significantly after informing the patients about potential seizure-inducing effects of the activation method; this was seen both in patients with only psychogenic non-epileptic seizures and in patients or

with both psychogenic non-epileptic and epileptic seizures<sup>90</sup>. Specifically, in the informed group 17.6% (6/34) of patients showed psychogenic non-epileptic seizures due to the IPS, two thirds (4/6) of them exclusively during the IPS.

#### 3.5.3 Other provocation methods

We did not find evidence for supporting standard use of provocation methods other than hyperventilation and IPS in routine EEG recordings <sup>72–80</sup>. Two main indications of other provocation methods were recognized: genetic generalized epilepsies with reflex trait and focal-onset epilepsies with a specific seizure trigger. Three category III observational studies compared the provocative effect of cognitive tasks to that of sleep deprivation, IPS and hyperventilation on interictal epileptiform discharges in juvenile myoclonic epilepsy<sup>72–74</sup> and two in genetic generalized epilepsies<sup>75,76</sup>. The duration of cognitive protocol was at least 15 minutes, typically over 30 minutes. The yield of cognitive tasks may exceed that of hyperventilation and IPS, but not sleep <sup>75,76</sup>. Seizures during cognitive testing were not observed in two studies<sup>74,75</sup> whereas they occurred in three studies<sup>72,73,76</sup>. In patients with juvenile myoclonic epilepsy, cognitive tasks were more provocative of myoclonia than conventional methods<sup>72,73,76</sup>.

Other category II-III studies investigated provocative effect of visual pattern stimulation in unselected patients of four to 12 years of age<sup>77</sup> and in pediatric patients with visually induced seizures<sup>78</sup>, and olfactory stimuli in mesial temporal lobe epilepsy<sup>79</sup> that did not increase the diagnostic utility of routine EEG.

#### 3.5.4 Recommendation

We conclude that the quality of evidence for hyperventilation to provoke epileptiform discharges is moderate despite study limitations (three consistent category I observational studies), but low for photic stimulation and other types of stimulation. Our conditional recommendation was formulated by modified Delphi discussions. Summary of provocation methods in shown in Table 3. We suggest

that hyperventilation, photic stimulation including baseline recording of eyes open, and eyes closed are part of routine or sleep EEG unless contraindicated. Asking the patient to blink, close and open eyes for several seconds documents artifacts, permits evaluation of posterior dominant rhythm and is a provocative method for eye-closure sensitivity<sup>100</sup>. We suggest tailoring the activation methods, and to use other simple stimulation methods, for example touch, sudden noises or reading aloud a difficult text, when they are known to provoke seizures<sup>4</sup>.

The patient and caregiver should be informed in advance about the potential benefits as well as adverse effects of activations, particularly seizures and potential loss of driving permission.

Information may also increase the occurrence of non-epileptic seizures. Patient has the right to know about the possibility to refuse activations.

The EEG technologist is responsible for the safety of the patient and the quality of recording that necessitates monitoring of one recording at a time. The patient should be under continuous surveillance during the recording. The EEG technologist should have possibility to call for help. During seizures, it is advisable to test the patient with a standardized method. We advise to use simplified versions of the ILAE guideline and UK national guideline for testing patients during seizures in long-term video EEG (Table 5)<sup>101,102</sup>. For testing of a potential absence seizure during generalized spike-andwave discharge longer than 3-4 seconds, we propose the method proposed by the ILAE Neurophysiology Task Force "The role of EEG in the diagnosis and classification of the epilepsy syndromes: a tool for clinical practice"<sup>4</sup>. EEG technologist gives simple commands or words when the generalized discharge starts and continues during the length of absence. Patients are monitored for a spontaneous response and after the offset of discharge, asked what they were told.

In adults, we propose to perform IPS before hyperventilation at the beginning of EEG at least 3 minutes apart<sup>71</sup>. However, if the referral diagnosis is genetic generalized epilepsy, it is advisable to do

activations at the end of recording due to increased probability of seizures. IPS often raises level of vigilance and decreases probability of sleep and hyperventilation has an opposite effect<sup>103</sup>. Therefore, in children, we advise performing hyperventilation at the beginning of sleep EEG and IPS at the end.

#### 3.5.4.1 Hyperventilation protocol

The patient is instructed to breathe deep 15-30 times/minute at least three minutes. In children, a pinwheel is useful to enhance breathing. In some patients, numbness or tingling of perioral region and fingers may occur; if so, this is not a reason to discontinue hyperventilation. The EEG technologist should encourage the patient and rate breathing effort adequate or inadequate. It is preferable to record two minutes of awake EEG after hyperventilation in all patient groups.

Contraindications for hyperventilation are sickle cell disease or trait, Moya-Moya disease and syndrome, cerebrovascular malformations including aneurysms, cerebrovascular events in the last three months, raised intracranial pressure, myocardial infarction, cardiac arrhythmias and other severe forms of cardiac disorders, severe pulmonary disorders, and pregnancy. Preferably, a list of contraindications is available for the referring physician to report existing contraindication. As a minimum and in cases of a time lag between referral and EEG, EEG technologist should inquire the patient about contraindications and document the answer.

#### 3.5.4.2 Intermittent photic stimulation protocol

We suggest to perform the IPS in accordance with the ILAE guideline on revisited methodology of photic stimulation in EEG recording<sup>71</sup>. There is no need to repeat IPS during the same EEG recording if it remains unequivocal. Contraindication for the IPS is pregnancy due to high risk of seizure.

#### 3.6 Conclusions

Routine and sleep EEG have an established role in clinical diagnosis of epilepsy and provide real-time evidence of brain dysfunction. However, the overall quality of evidence for recording standards of routine and sleep EEG is low, which is an important limitation. This paper is the second joint IFCN-ILAE

EEG guideline in addition to recently published "Minimum standards for inpatient long-term video-electroencephalographic monitoring: A clinical practice guideline of the International League Against Epilepsy and International Federation of Clinical Neurophysiology<sup>104</sup>. The minimum standards summarize the available evidence based on systematic review and provides the first expert consensus-based global standards to record EEG (Table 6). Although the recommendations are conditional, they provide a feasible international standards for new EEG laboratories and challenge established EEG laboratories to evaluate their protocols and to tailor implementation strategies of recommendations to the local context<sup>105</sup>. In the future, further research development and diagnostic accuracy studies are needed, as well as studies addressing cost-efficacy of routine and sleep EEG.

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#### Disclosure of Conflicts of Interest

Sándor Beniczky has served as scientific consultant for Epihunter and received speaker honoraria from Natus. Jonathan J. Halford has served as a Board Advisor for CortiCare. Ronit M Pressler is an investigator for studies with UCB and does consultancy work for Kephala, Ireland. She served as a speaker and/or on Advisory Boards for Natus, GW Pharmacceuticals, Esai, and UCB. The remaining authors have no conflicts of interest

#### **Ethical Publication Statement**

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

**Table 1.** Clinical questions and Patient/population, Intervention, Comparison and Outcome (PICO) statements.

Question	n	Population	Intervention	Comparison	Outcomes
1.	What are the indications for routine and sleep EEG?	Patient in EEG	EEG recording	No EEG recording	Impact on diagnostics, management decisions or prognostication
2.	What are the minimum technical standards for routine and sleep EEG?	Not practically a	applicable		
3.	What provocation methods should be used in routine and sleep EEG and how?	Patient in EEG	Photic stimulation Hyperventilation Other provocation	No provocation	Epileptiform abnormality Seizure -epileptic -non-epileptic Adverse effects
4.	What should be a minimum duration of routine and sleep EEG to be optimally diagnostic?	Patient in EEG	EEG duration 1	EEG duration 2	Abnormal EEG finding
5.	Should sleep deprivation (partial or all night/24h) used to obtain sleep?	Patient in EEG	Sleep deprivation	Natural sleep	Sleep Adverse effects Cost-benefit
6.	Can melatonin or other drugs be used for sleep induction?	Patient in EEG	Melatonin Other sleep- inducing drug	Sleep deprivation Sleep inducing drug	Sleep Adverse effects Cost-benefit

EEG, electroencephalography

 Table 2. Indications of non-emergent electroencephalography (EEG) recorded by appointment

Epilepsy-related indications	Other indications for differential diagnosis
Clinical suspicion of seizure or epilepsy	Psychogenic non-epileptic seizures
Reconsideration of the initial diagnosis of epilepsy	Paroxysmal behavioral changes
Syndromic classification of epilepsy	Suspected encephalopathy
Changes in seizure pattern (seizure type or semiology)	Acute or subacute dementia
Etiological evaluation of epilepsy	
Prior to tapering of AED in seizure free patients	
Systematic follow up of specific epileptic syndromes (for example infantile epileptic spasms syndrome and epileptic encephalopathy with spike-and-wave activation in sleep)	

Table 3. Summary of minimum standards for recording routine and sleep electroencephalography (EEG)

Electrode types	Gold or silver/silver-chloride cup electrodes applied with electrode paste or gel, electrode caps, MRI compatible electrodes and needle electrodes in certain circumstances			
Electrode array	The 25-electrode IFCN montage, when possible. Otherwise: 10-20 array.			
Polygraphic channels	One ECG At least two EMG channels if motor events of clinical interest are suspected At least two EOG channels if assistance is needed in differentiation between eye movement and slow EEG activity			
Electrode impedances	< 5 k $\Omega$ is recommended < 10 k $\Omega$ is considered acceptable			
Minimum sampling rate	256 Hz			
Filtering for Visualization: EEG EOG EMG	High pass 0.5 Hz; Low pass 70 Hz High pass 0.3 Hz; Low pass 35 Hz High pass 10 Hz; Low pass 100 Hz			
Video	At least one camera when events of clinical interest are suspected			
Display	Resolution 7 μV/mm for adults' EEG, 10uV/mm for children's EEG Possibility to adjust viewing settings, gain of each channel, time resolution, filters and annotations Possibility to display voltage maps			
Data storage	The entire EEG and video from clinical events			
Data export	Comma Separated Value data format (CSV) or European data format (EDF) or Digital Communication in Medicine (DICOM) format			
Duration of recording	Routine EEG 20 min Sleep EEG 30 min Individualize the sleep EEG recording time and duration when increased benefit is expected. Postprandial period increases the chances of sleep in infants and children.			
Sleep induction	Partial sleep deprivation for adults and children ≥ 12 years of age Melatonin or sleep deprivation in children < 12 years of age Dose of melatonin: 1-3 mg administered 30-60 min before EEG recording. If melatoni is not available, chloral hydrate may be used when partial sleep deprivation fails to attain sleep.			
Hyperventilation (HV)	At the beginning of routine or sleep EEG $\geq$ 3 min after IPS. Exceptions: if EEG indication is genetic generalized epilepsy, perform HV at the end of recording. Record 2 min awake EEG after HV.			

	Method: 15-30 deep breaths /min for ≥ 3 min In children, a pinwheel windmill is useful to enhance breathing. The EEG technologist should encourage the patient and rate breathing effort adequate or inadequate. Use a checklist for contraindications. Test the patient if a seizure occurs.
Intermittent photic stimulation (IPS)	Perform IPS at the beginning of routine or sleep EEG $\geq 3$ min before HV. In children, perform IPS at the end of sleep EEG. Method: ILAE guideline on revisited methodology of photic stimulation* - stop the visual stimulus immediately as soon as generalized epileptiform discharges occur. Photomyogenic reaction must not be mistaken for a seizure use flash frequencies: $1-2-8-10-15-18-20-25-40-50-60$ Hz. If there is a generalized response at a certain frequency (lower threshold), skip the remainder of the series and start again with 60 Hz and go down in frequencies ( $60-50-40-25$ Hz) until again a generalized photoparoxysmal response occurs (upper threshold) determine IPS sensitivity with separate trains of flashes of 5 s duration each during eye closure, eyes closed, and eyes open. If limited in time, choose the closure of the eyes on command at the start of a flash train and stimulate for 7 s per flash frequency observe clinical signs and test seizures Contraindication: pregnancy
Asking the patient to blink, close and open eyes for several seconds	At the beginning of routine EEG In wake period at the end of sleep EEG (assessment of posterior dominant rhythm) Assisted eye closure may be needed in children.

<sup>\*</sup>Kasteleijn-Nolst Trenité D, Rubboli G, Hirsch E, Martins da Silva A, Seri S, Wilkins A et al. Methodology of photic stimulation revisited: Updated European algorithm for visual stimulation in the EEG laboratory. Epilepsia, 53(1):16–24, 2012.

MRI, magnetic resonance imaging; IFCN, International Federation of Clinical Neurophysiology; ECG, electrocardiography; EMG, electromyography; EOG, electro-oculography; IPS, intermittent photic stimulation

**Table 4.** Proposed partial sleep deprivation protocol for sleep electroencephalography (EEG) in morning time

Age group	Children aged < 6 year	Children aged 6-12 years	Children aged > 12 years	Adults
Instructions	Shorten the sleep by 1-3 hours or an amount that you estimate is necessary for falling asleep at the time of EEG.	Go to sleep two hours later than usual and wake up two hours earlier than usual. Stay awake until the EEG.	Go to sleep two hours later than usual, but at the latest at 00 AM. Stay awake from 04 AM until the EEG.	Go to sleep at 00 AM. Stay awake after 04 AM until the EEG.

**Table 5. Proposed** protocol for testing patients during seizures in routine and sleep electroencephalography (EEG)

Children < 6 years old Children ≥ 6 years old and adults 1. Say the patient's first name 1. Say the patient's first name 2. "Are you ok? o If reacting, ask: "What do you feel?" 3. "Lift both arms up/like Superman or touch toy with right o If not, touch arm & left hand/ clap." 2. "Lift arms." First say only, if not reacting show o First say only, if not reacting show 4. Postictally ask: 3. "Please repeat and remember the following words: horse, "Did you know what just happened?" table (for example) 4. Postictally ask: "Did you have a seizure?" "Can you describe what happened?" "What did you feel right before/at the beginning of the "Can you recall the words I said to you/what I asked to do?"

For testing of a potential absence seizure during generalized spike-and-wave discharge longer than 3-4 seconds, we suggest giving commands or words when the generalized discharge starts and continues during the length of absence. Patients are monitored for a spontaneous response and after the offset of discharge, asked what they were told.

Modified from Beniczky S, Neufeld M, Diehl B, Dobesberger J, Trinka E, Mameniskiene R, et al. *Epilepsia*. 2016; 57(9), Wiley Periodicals, Inc. and Pressler R, Seri S, Kane N, Martland T, Goyal S, Iyer A, et al. *Seizure*. 2017; 50, Elsevier.

## **Table 6.** Summary statements of the minimum standards for recording routine and sleep electroencephalography EEG

**Indications of non-emergent EEG** recorded by appointment include indications related to epilepsy, seizures, brain dysfunction and differential diagnosis as detailed in Table 2.

Technical standards are summarized in Table 3.

**Duration of EEG:** 20 minutes for the routine EEG and 30 minutes for the sleep EEG excluding preparation is suggested. It is advisable to book the sleep recording of infants and children in the postprandial period, where there is a higher chance to fall asleep.

We suggest individualizing the recording time and duration when increased benefit is expected. Booking morning time for patients with suspected juvenile myoclonic epilepsy, prioritizing sleep recording in patients with suspected or diagnosed self-limited focal epilepsy of childhood or infantile epileptic spasms syndrome, and on suspicion of infantile epileptic spasms syndrome, extending recording at least 10 minutes after awakening to increase the probability of recording of epileptic spasms probably increase the yield of EEG.

**Sleep-induction:** Partial sleep deprivation is suggested as a primary method in adults and children 12 years of age or older who can cooperate to the sleep deprivation. An example of suggested partial sleep deprivation protocol is shown in Table 4.

However, it is important to note that there are no studies evaluating the safety of partial or full sleep deprivation for any age group. Sleep deprivation may also cause significant distress to a child and family. Melatonin or sleep deprivation are suggested as a primary sleep induction method in children under 12 years of age. If sleep deprivation or melatonin fails to induce sleep, their combination may be more effective. Melatonin is proposed as a primary sleep induction method in children and adults who cannot cooperate to partial sleep deprivation. The suggested dose of melatonin is 1-3 mg administered 30-60 min before the start of the EEG recording. If melatonin is not available in the market, chloral hydrate may be used when partial sleep deprivation fails to attain sleep and patient safety is ensured.

**Provocation methods**: Hyperventilation, intermittent photic stimulation (IPS) including baseline recording of eyes open, and eyes closed are suggested unless contraindicated. Asking the patient to blink, close and open eyes for several seconds documents artifacts, permits evaluation of posterior dominant rhythm and is a provocative method for eye-closure sensitivity. It is proposed to use other simple stimulation methods, for example touch, sudden noises or reading aloud a difficult text, when they are known to provoke seizures.

In adults, IPS is suggested to perform before hyperventilation at the beginning of EEG at least 3 minutes apart. However, if the referral diagnosis is genetic generalized epilepsy, it is advisable to do activations at the end of recording due to increased probability of seizures. IPS often raises level of vigilance and decreases probability of sleep and hyperventilation has an opposite effect. Therefore, in children, it is useful to perform hyperventilation at the beginning of sleep EEG and IPS at the end.

The patient and caregiver should be informed in advance about the potential benefits as well as adverse effects of activations, particularly seizures and potential loss of driving permission. Information may also increase the occurrence of non-epileptic seizures. Patient has the right to know about the possibility to refuse activations.

Hyperventilation and IPS protocols are detailed in Table 3.

Contraindication for IPS: pregnancy

Contraindications for hyperventilation are sickle cell disease or trait, Moya-Moya disease and syndrome, cerebrovascular malformations including aneurysms, cerebrovascular events in the last three months, raised intracranial pressure, myocardial infarction, cardiac arrhythmias and other severe forms of cardiac disorders, severe pulmonary disorders, and pregnancy. Preferably, list of contraindications is available for the referring physician to report existing contraindication. As a minimum and in cases of a time lag between referral and EEG, EEG technologist should inquire the patient about contraindications and document the answer.

Responsibility of EEG technologist is to guarantee the patient safety and the quality of recording that necessitates continuous monitoring of one recording at a time. The patient should be under continuous surveillance during the recording. The EEG technologist should have possibility to call for help. During seizures, it is advisable to test the patient with a standardized method (Table 5).

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