ORIGINAL RESEARCH

# Determining the Spike–Wave Index Using Automated Detection Software

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**Purpose:** The spike–wave index (SWI) is a key feature in the diagnosis of electrical status epilepticus during slow-wave sleep. Estimating the SWI manually is time-consuming and is subject to interrater and intrarater variability. Use of automated detection software would save time. Thereby, this software will consistently detect a certain EEG phenomenon as epileptiform and is not influenced by human factors. To determine noninferiority in calculating the SWI, we compared the performance of a commercially available spike detection algorithm (P13 software, Persyst Development Corporation, San Diego, CA) with human expert consensus.

**Methods:** The authors identified all prolonged EEG recordings for the diagnosis or follow-up of electrical status epilepticus during slow-wave sleep carried out from January to December 2018 at an epilepsy tertiary referral center. The SWI during the first 10 minutes of sleep was estimated by consensus of two human experts. This was compared with the SWI calculated by the automated spike detection algorithm using the three available sensitivity settings: "low," "medium," and "high." In the software, these sensitivity settings are denoted as perception values.

**Results:** Forty-eight EEG recordings from 44 individuals were analyzed. The SWIs estimated by human experts did not differ from the SWIs calculated by the automated spike detection algorithm in the "low" perception mode ($P = 0.67$). The SWIs calculated in the "medium" and "high" perception settings were, however, significantly higher than the human expert estimated SWIs (both $P < 0.001$).

**Conclusions:** Automated spike detection (P13) is a useful tool in determining SWI, especially when using the "low" sensitivity setting. Using such automated detection tools may save time, especially when reviewing larger epochs.

**Key Words:** ESES, Electrical status epilepticus during slow-wave sleep, SWI, Automatic spike detection, Automated spike detection.

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A key feature in the diagnosis of electrical status epilepticus during slow-wave sleep (ESES) is the amount of epileptiform activity occurring during sleep, usually expressed as a "spike–wave index" (SWI).[1] In 1971, ESES was originally described as an epileptic encephalopathy characterized by sleep-induced activation of epileptiform activity on the EEG.[2] In 1989, the International League Against Epilepsy (ILAE) defined the characteristic EEG pattern in ESES as continuous diffuse spike–waves during slow-wave sleep.[3] This condition mainly affects children and is associated with cognitive decline involving a wide spectrum of developmental and neurocognitive domains.[4] The underlying etiology can be structural or genetic.[5]

The ILAE definition of ESES does not include a specific cut-off percentage regarding the amount of epileptiform activity in the EEG. A recent guideline, however, suggested a criterion of at least 50% epileptiform activity during sleep, especially if the clinical symptoms are compatible with an ESES-related syndrome.[6] The same guideline also mentions a cut-off of at least 85% epileptiform activity, mainly to facilitate comparison with existing literature. The methods used to determine the SWI varies, especially regarding the amount of sleep EEG which is analyzed (from 100 seconds to a whole sleep cycle).[6,7]

Automated spike detection algorithms have long been available.[8] They are useful in reviewing EEG recordings by detecting interictal epileptiform discharges, to quantify spike density, and possibly to distinguish different epileptiform morphologies.[9] Experts' confidence in these systems are, however, low.[10] Future users need independent research with this software to gain confidence. An issue in validating such algorithms is the lack of a gold standard in EEG review, mainly because of large interrater and intrarater variability seen in identifying spikes or sharp waves in the same EEG recording.[11] Factors that play a role are, for example, reader style, fatigue, and loss of concentration. The lack of an objective gold standard creates difficulties in assessing whether a detection algorithm is performing well.[12]

The Persyst 13 (P13) is one of the available software packages for EEG visualization that has an automated spike and seizure detection feature. The spike detection algorithm is a neural network that attempts to mimic the perception-based marking of human experts (HEs).[13,14] For users, the precise details of the algorithm and the neural network rules are mostly unknown except for some technical aspects.[14] The algorithm uses different sensitivity settings to present the output; these are denoted as perception values, ranging from zero to one. Ambiguous epileptiform features are assigned near-zero values, and clear epileptiform abnormalities are assigned near-one values.[13] P13 has three different settings: "high," "medium," and "low." The "high" setting has a perception threshold setting of 0.1, the "medium" of 0.4, and the "low" of 0.9.

Counting spikes manually is a time-consuming task.[15] Estimating the SWI using automated detection software could

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**TABLE 1.** Median SWI (in %) of All Recordings ($N = 48$)

| | Median SWI in % | Range (%) Min | Range (%) Max | Percentile Q1 | Percentile Q3 | P13 Difference From HE (*P*) |
|---|---|---|---|---|---|---|
| HE consensus | 18 | 0 | 99 | 0 | 80 | |
| P13 (low*) | 16 | 0 | 96 | 1 | 78 | 0.67 |
| P13 (medium*) | 28 | 1 | 98 | 6 | 82 | <0.001 |
| P13 (high*) | 36 | 3 | 99 | 36 | 83 | <0.001 |

*Perception setting, P13, Persyst 13 spike detection.
HE, human experts; SWI, spike–wave index.

**TABLE 2.** Median SWI (in %) of Recordings Containing Spikes ($N = 28$)

| | Median SWI in % | Range (%) Min | Range (%) Max | Percentile Q1 | Percentile Q3 | P13 Difference From HE (*P*) |
|---|---|---|---|---|---|---|
| HE consensus | 76 | 1 | 99 | 52 | 92 | |
| P13 (low*) | 75 | 2 | 96 | 51 | 88 | 0.19 |
| P13 (medium*) | 79 | 6 | 98 | 61 | 93 | <0.001 |
| P13 (high*) | 79 | 11 | 99 | 64 | 94 | <0.001 |

*Perception setting, P13, Persyst 13 spike detection.
HE, human experts; SWI, spike–wave index.

save time, as a detection algorithm is able to calculate a SWI in few seconds (after the record is processed). This is independent of the size of the epoch. Thus, the time saved is larger when reviewing longer EEG recordings. Thereby, an automated detection algorithm will consistently detect a certain EEG phenomenon as epileptiform and is not influenced by individual reader style or other reader factors such as fatigue. A recent report found that the software-calculated SWI using P13 was noninferior to experts' estimates.[16] This report, however, was based on a small number of nonheterogeneous recordings from ESES patients. Thereby, the "high" perception setting was used instead of the "medium" setting, which the Persyst Development Corporation states is the default mode. Furthermore, this report did not provide information about accurate quantification of lower SWIs, which can be useful for follow-up of patients. The algorithm, therefore, needs further validation.

In this study, we compared the performance of the P13 algorithm versus HE consensus in a heterogeneous set of recordings, reviewing all three perception value settings ("high," "medium," or "low").

## METHOD

All prolonged EEG recordings made with an ESES or follow-up of ESES referral question in children or teenagers (age 0–18 years) between January 1, 2018 and December 31, 2018 were included. Informed consent was not obtained because of the study's retrospective nature. Thereby, only anonymized data, and no video data, were used. This study was approved by the institutional review board.

The HEs were a clinical neurophysiologist and a physician assistant each with more than five years of experience in reviewing EEGs. The education of this particular physician assistant contained multiple years of medical training combined with dedicated EEG training, supervised by board-certified clinical neurophysiologists. The HEs were masked to the initial video-EEG monitoring report. The two HEs reviewed the EEGs together and only viewed the first 10 minutes of NREM sleep (starting point at 50% decrease of posterior dominant rhythm, appearance of lateral eye movements or drowsiness, and/or vertex waves). They estimated a SWI for each recording defined as the average percentage of each 1-second epoch containing the sharp component of an epileptiform discharge. Interictal epileptiform discharges were defined as paroxysmal, sharply contoured, wave forms, clearly distinguished from the background activity, had a field, and a duration of less than 200 milliseconds.[17] In the SWI estimation, both generalized and focal discharges were included. Both experts had to agree on the presence of the interictal epileptiform discharge for it to be counted. The SWI was estimated without explicit time constraints, and the EEG traces could be reformatted as in the clinical setting. All EEGs were reviewed with the SystemPLUS Evolution software (Micromed, Veneto, Italy) using standard 10 to 20 International electrode recording and 256 Hz sample frequency. The time of the manual count by the HEs was measured for each EEG record.

For the automated spike detection, we used the P13 software (Persyst Development Corporation, San Diego, CA). The SWI was calculated using all three different perception settings. An SWI calculated by the detection software was also defined as the average percentage of each 1-second epoch that contained an epileptiform discharge.

Continuous variables were analyzed using the Wilcoxon signed rank test for nonparametric data using SPSS (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY).

## RESULTS

A total of 48 recordings from 44 patients (24 male) were identified. The mean patient age was 7.8 years (SD 2.4 years; range, 3–11 years).

Human experts estimated an SWI in a median time of 4 minutes 54 seconds (range, 30 seconds–14 minutes 37 seconds) per record. According to the HEs, 28 recordings included spikes.

The SWIs estimated by the HEs did not significantly differ from the SWI calculations of the algorithm in the "low" perception settings (Tables 1 and 2). The SWI estimated by the HEs differed significantly from the "medium" perception settings and the "high" perception settings. The SWIs calculated in these modes were higher than the HE-estimated SWIs.

The largest difference in calculated SWI within one subject in the "low" perception setting was 10% (the P13 algorithm calculated 51% vs. 61% for the HEs). The largest difference in calculated SWIs within an individual between the P13 algorithm in the "medium" setting was 18% and in the "high" perception setting was 29%. The differences between SWIs calculated by HEs and the three perception settings were, in most cases, smaller for the higher SWIs (especially above 70%) than in the lower SWIs. This is shown in Fig. 1.

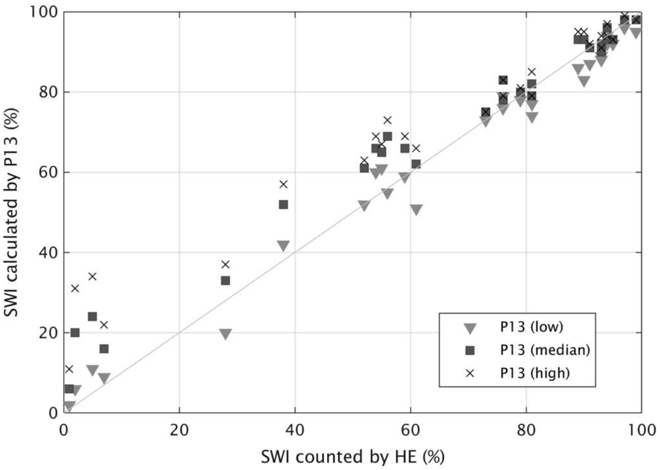


**FIG. 1** SWI Calculated by HEs and P13. HE, human experts; P13, Persyst 13 spike detection; SWI, spike–wave index.

Based on the SWIs estimated by the HEs, 22 recordings met the ESES criteria of $\geq$ 50% of 1-second epochs containing spikes (Table 3). All were also identified with an SWI $\geq$ 50% by the P13 algorithm using the "low" setting: thus, sensitivity was 100% (confidence interval, 82%–100%) and specificity was also 100% (confidence interval, 52%–100%). In one recording, the algorithm in "medium" and "high" settings calculated a SWI $\geq$ 50%, where the HEs calculated a SWI <50%: thus, in "medium" and "high" perceptions settings, the sensitivity is 100% (confidence interval, 82%–100%) and the specificity is 83% (confidence interval, 36%–99%).

No spikes were seen by HEs in 20 recordings. The algorithm, however, detected spikes in most of these recordings. It calculated SWIs ranging from 0% to 6% in the "low" setting, from 1% to 20% in the "medium" setting, and from 3% to 33% in the "high" setting.

**TABLE 3.** Number of Records Meeting ESES Criteria, Calculated by HEs and by P13

| | P13 (Low*) | | P13 (Medium and High*) | |
|---|---|---|---|---|
| | P13 ≥50% | P13 <50% | P13 ≥50% | P13 <50% |
| HE ≥ 50% | 22 | 0 | 22 | 0 |
| HE >0% and <50% | 0 | 6 | 1 | 5 |

*Perception setting, P13, Persyst 13 spike detection.
HE, human experts; ESES, electrical status epilepticus during slow-wave sleep.

## DISCUSSION

We showed that calculating SWI using the spike detection algorithm P13 in the "low" perception setting is non-inferior to estimating SWI by HEs. The perception setting matters especially in the lower SWIs because the differences between the settings are small in the higher SWIs.

We also showed that using the spike detection software may save HEs time in comparison with human estimation. Thereby, the software makes it easy to estimate SWI for larger epochs, such as a first sleep cycle or even a whole night. Another advantage is that the algorithm will always detect the same event as epileptiform and thus eliminate human factors such as reader style or fatigue.

There are limitations to our study. We tried to generate a heterogeneous dataset with SWIs in all ranges. There were, however, few recordings with an SWI around the cut-off point of 50%. At group level, the SWI estimated by HEs and the P13 in "low" perception setting did not differ, but we did see some individual differences between the calculated SWIs. In practice, this can mean the difference in reaching or not reaching the criterion of at least 50% epileptiform activity. However, in ESES-related syndromes, the SWI is only part of the diagnostic criteria, as the clinical symptoms are also taken into account. Thereby, the SWI criterion of 50% is arbitrary. Another issue when testing the reliability of a spike detection algorithm is that the interrater agreement between EEG reviewers is low, so our HE estimated SWI is not the gold standard. We approached this by estimating the SWI in consensus, instead of using a single individual to estimate SWIs (which is current practice in our center).

A disadvantage of using this algorithm is that it has false detections—usually sharp physiologic sleep phenomena, especially K-complexes. This was especially noticeable in (near-) normal EEG recordings. The P13 calculated SWI of these normal EEGs is up to 6% in "low" perception settings and up to 33% in "high" perception settings and reviewers must always be aware of this especially when reviewing EEGs of children, who often have sharp sleep phenomena.

Spike detection software is an useful tool in obtaining SWI and can help reducing the burden of manual estimation. Further validation of the software is needed in larger cohorts, multiple centers, and by multiple HEs.

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