ABSTRACT The decreasing trend in power spectral density (PSD) of electroencephalogram (EEG) has been shown to be related with the depth of anesthesia (DOA). However, conventional DOA indices, which utilize part of EEG frequency band, have a difficulty in quantifying the decreasing trend in the EEG PSD along the frequency axis. This paper proposes a method of effectively quantifying the characteristic change in the EEG PSD to measure the DOA. The method is based on the newly introduced ordinal PSD (O-PSD) which assigns ordinal indices to a series of values in the order of PSD magnitude. The O-PSD can capture the spectral trend along the overall frequency band robust to the EEG variation due to inter-subject dependency and measurement environment. We quantified the O-PSD pattern into a unitless index in the range 0 to 1. We compared the proposed O-PSD based index with the conventional indices for 15 subjects with injection rate of 12 mg/kg/h and 12 subjects with injection rate of 6 mg/kg/h. We evaluated the discriminative performance of the proposed index using prediction probability and Spearman’s correlation coefficient. Also, we evaluated the steadiness and stability of the proposed index using the coefficient of variation. Our proposed index was shown to be superior in distinguishing consciousness and unconsciousness, and a stable and steady measure during unconsciousness. These results indicate that the O-PSD and the proposed index would be a reliable method for quantifying the DOA.

INDEX TERMS Depth of anesthesia, EEG, ordinal representation, power spectral density.
to measurement error, which may lead to inaccuracy in quantifying the DOA. Additionally, although recent studies have shown that a decreasing trend in the EEG PSD along the frequency axis is related to the DOA [18]–[23], the conventional indices that utilize the specific frequency bands of the EEG PSD have difficulty in quantifying the decreasing trend of the EEG PSD along the overall frequency axis.

In this paper, by newly introducing an ordinal PSD (O-PSD), we quantify the changes in the trend of the EEG PSD. The O-PSD, which assigns ordinal indices to a series of values in the order of the PSD magnitude, can measure the spectral trend along the overall frequency band in a manner that is robust to EEG variation due to inter-subject dependency and measurement environment. Also, the O-PSD provides a unit-less measure in the range 0 to 1. In the experimental results, we demonstrate that the O-PSD can be useful for measuring the DOA during the GA process.

II. METHODS

A. SUBJECTS

After obtaining the approval of the Review Board of the Asan Medical Center, 27 healthy volunteers over 20 years old were selected for the EEG recording during GA. A subject with potential risks of adverse reaction to the anesthetic was excluded in advance. All subjects were well informed about the whole process, and signed a written informed consent. Two groups of subjects with different injection rate were randomly organized. First group of 15 subjects were injected at 12 mg/kg/h, and second group of 12 subjects were injected at 6 mg/kg/h.

B. ANESTHESIA PROCESS

Microemulsion propofol (Aquafol-MCT™, Daewon Pharm. Co. Ltd., Seoul, Korea) was infused intravenously through an 18 G angiocath for the GA [24]. The anesthetic was constantly infused for an hour. The plasma concentration of the subjects was checked at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 15, 20, 30, 40, 50, 58, 60, 62, 66, 70, 80, 90, and 120 min after the infusion of the propofol. Additionally, the plasma concentration of the propofol was checked at loss of consciousness (LOC) and recovery of consciousness (ROC). LOC was the first time when a subject did not respond to a verbal command. The command was “Open your eyes”, and was repeated from the induction to the LOC every 10 s. ROC was the first time when the subject again responded to the verbal command. The command was repeated from the end of infusion to the ROC every 10 s. The subjects were preoxygenated with 100 % oxygen, and then oxygenated at 4 L/min during the GA. To check the state of the subjects during the GA, the recording proceeded under monitoring of electrocardiography, end-tidal carbon dioxide partial pressure, pulse oximetry, and non-invasive blood pressure. More details of the anesthesia process are described in [25].

C. EEG RECORDINGS

The EEG was recorded at 7 frontoparietal regions (Fp1, Fp2, F3, F4, P3, P4, and Cz with reference electrode at A2 according to the international 10-20 system) with QEEG-8 (Laxtha Inc., Daejeon, Korea) at Fs = 256 samples/s. We used the recording of the F3 channel from the infusion to 120 min after the infusion.

D. PROPOSED ORDINAL PSD (O-PSD)

As the plasma concentration of the propofol increases (Fig. 1(a)), the slow and simple oscillated EEG turns into the fast and complex oscillated EEG (Figs. 1(b) and (d)). In the EEG PSD, the spectral powers in low frequency increase, while those in high frequency decrease (Figs. 1(c) and (e)). However, it is hard to quantify the change in trend of the EEG PSD. The wide dynamic range and variation of the spectral powers due to the subject and measurement environment hinder capturing the change in the EEG PSD. We propose the O-PSD, which helps to clearly identify the change in the trend of the EEG PSD by ordering the magnitude of the EEG PSD.

The EEG PSD, p(fk) is calculated using the discrete Fourier transform as in (1).

\[
X(f_k) = \sum_{n=1}^{N} x(n) \cdot \exp\left(-\frac{j2\pi kn}{N}\right),
\]

\[
f_k = \frac{k-1}{N} \cdot F_s, \quad k = 1, \ldots, N,
\]

\[
p(f_k) = \frac{|X(f_k)|^2}{N}, \quad (1)
\]

where, x is the amplitude of the EEG, and N is the length of the EEG.

The proposed O-PSD, \( \hat{p}(f_k) \) is simply calculated as

\[
\hat{p}(f_k) = \frac{1}{N-1} \sum_{i=1}^{N} I(p(f_k) > p(f_i)) \quad k = 1, \ldots, N, \quad (2)
\]

where, \( I(\text{statement}) = \begin{cases} 1 & \text{if statement = true} \\ 0 & \text{if statement = false} \end{cases} \)

Figure 2 shows simulated examples of the PSD and the corresponding O-PSD. Figure 2(a)-(e) are the PSDs with various trends, while Figs. 2(f)-(j) are the corresponding O-PSDs.

Examples in Figs. 2(c)-(e) show decreasing and increasing trends of the PSD, and we can observe that such trends hinder capturing the change in the EEG PSD. Additionally, the plasma concentration of the propofol. Moreover, the plasma concentration of the propofol and the EEG PSD have difficulty in quantifying the decreasing trend of the EEG PSD along the overall frequency axis.
Second, the O-PSD maps the largest and the smallest values to 1 and 0, respectively. Figure 3 shows single subject’s EEG PSDs and the corresponding O-PSDs over the GA. Unlike the EEG PSDs in Fig. 3(a), we can clearly observe that the O-PSDs in Fig. 3(b) are dispersed widely between 0 and 1 over the frequency when the subject is awake. As the anesthesia deepens, a decreasing and diagonal pattern gradually appears in the O-PSD. We used the absolute value of Pearson’s correlation coefficient (Corr) to quantify the pattern of the O-PSD. The Corr is low when the O-PSD is dispersed, and becomes high as the O-PSD is diagonalized. Figure 3(c) shows that the Corr increases near the LOC, maintains high during unconsciousness, and decreases near the ROC over the GA process.

III. RESULTS

We compared the proposed O-PSD based index with the conventional indices for 15 subjects with injection rate of 12 mg/kg/h, and 12 subjects with injection rate of 6 mg/kg/h. For comparison purpose, the RBR, SEF95, ApEn, and SFS are used as the conventional indices.

Figure 4(a) shows the change of the indices over the GA of a single subject with injection rate of 12 mg/kg/h. After the plasma concentration of the propofol increased to about 4 µg/mL, the subject lost consciousness. Until the subject lost consciousness, the proposed index gradually increased, while the RBR, SEF95, ApEn, and SFS gradually decreased. After the end of the injection (60 min), the plasma concentration of the propofol rapidly decreased, and after
a few minutes, the subject recovered consciousness. Around the ROC, the proposed index started to decrease, while the RBR, SEF95, ApEn, and SFS started to increase. Figure 4(b) shows the change of indices over the anesthesia of a single subject with the injection rate of 6 mg/kg/h. As of 12 mg/kg/h, the indices with injection rate of 6 mg/kg/h showed an evident change near the LOC and the ROC. The difference was that the maximum plasma concentration of the propofol was lower than that of 12 mg/kg/h, and the change of the indices during the sedation was slower than those of 12 mg/kg/h.

To identify the change of indices over the GA of multiple subjects, we rearranged the indices of all subjects with the same injection rate around the time points at the LOC (tL), the ROC (tR), and the middle of unconsciousness (40 min...
FIGURE 4. Conventional indices and the proposed index of a single subject over the GA. (a) Indices of a single subject with injection rate of 12 mg/kg/h, and (b) indices of another single subject with injection rate of 6 mg/kg/h.

FIGURE 5. Median of conventional indices and the proposed index over the GA (the shaded face is bounded by the 25 percentiles and 75 percentiles of an index). (a) Median of the indices with injection rate of 12 mg/kg/h, and (b) median of the indices with injection rate of 6 mg/kg/h.

We evaluated the discriminative performance of the indices between consciousness and unconsciousness using the prediction probability ($P_k$) and Spearman’s correlation after the injection). Then we plotted the median, 25 percentiles, and 75 percentiles of the rearranged indices for the injection rate 12 and 6 mg/kg/h (Fig. 5).
TABLE 1. Prediction probability \( P_k \) with standard error and Spearman’s correlation coefficient \( r_s \) of the conventional indices and the proposed index (p-value for \( r_s \) of all the indices < 0.0005. For convenience of interpretation, we replaced \( P_k \) by \( 0.5 + |P_k - 0.5| \).

| Index | Injection rate [mg/kg/h] | \( P_k \) | \( r_s \) | \( P_k \) | \( r_s \) |
|-------|-------------------------|---------|---------|---------|---------|
|       | 12                      |         |         |         |         |
| Proposed | 0.965 (0.0025)         | 0.821     | 0.975 (0.0017) | 0.828 |
| RBR    | 0.823 (0.0033)         | -0.587     | 0.949 (0.0020) | -0.775 |
| SEF95  | 0.925 (0.0029)         | -0.765     | 0.956 (0.0019) | -0.781 |
| ApEn   | 0.885 (0.0031)         | -0.690     | 0.912 (0.0025) | -0.723 |
| SFS    | 0.911 (0.0030)         | -0.727     | 0.935 (0.0023) | -0.760 |

TABLE 2. CV of conventional indices and the proposed index.

| Index | Injection rate [mg/kg/h] | CV [%] | CV [%] |
|-------|-------------------------|-----|-----|
|       | 12                      | 30.47 | 24.92 |
|       | 6                       | 70.03 | 31.63 |
| Proposed | 33.07         | 27.81 |
| RBR    | 49.07         | 30.96 |
| SEF95  | 49.08         | 42.73 |

Coefficient \( r_s \). \( P_k \) is a nonlinear measurement of the ordinal association between two variables, and the most commonly used evaluation statistics of the DOA indicator [26]. \( P_k = 1 \) means the perfect positive ordinal association, \( P_k = 0.5 \) indicates no ordinal association between two variables, and \( P_k = 0 \) means the perfect negative ordinal association. Also, \( r_s \) is the non-parametric version of the Pearson’s correlation, which measures the association between two ranked variables [27]. \( r_s = 1 \) means the perfect positive correlation, \( r_s = 0 \) means the no correlation, and \( r_s = -1 \) means the perfect negative correlation between two ranked variables. To calculate the \( P_k \) and the \( r_s \), we randomly sampled 100 values of each index at consciousness and unconsciousness, respectively, from all subjects with same injection rate. As described in Table 1, \( P_k \) and \( r_s \) of the proposed index are higher than those of the conventional indices at injection rate of 12 and 6 mg/kg/h.

Although the median of the proposed index and the conventional indices were steady during unconsciousness, the distribution of the 25 and 75 percentiles of the indices differed by index (Fig. 5), i.e. the robustness to the inter-subject dependency or measurement environment differed by index. Thus, we quantified how stable the indices are during the unconscious state in terms of the coefficient of variation (CV) for all subjects in both groups with injection rate of 12 and 6 mg/kg/h, respectively. The CV, which is a standardized precision measurement for comparing the dispersion of distributions with different units [28], is calculated as

\[
CV = 100 \cdot \frac{\text{std}(\text{Idx}_{\text{uncon}})}{\text{mean}(\text{Idx}_{\text{con}}) - \text{mean}(\text{Idx}_{\text{uncon}})},
\]

where, \( \text{Idx}_{\text{con}} \) = values of an index in consciousness, \( \text{Idx}_{\text{uncon}} \) = values of an index in unconsciousness, \( \text{mean}(x) \) = arithmetic mean of \( x \), \( \text{std}(x) \) = standard deviation of \( x \). Table 2 shows that the CV of the proposed index during unconsciousness is lowest at the injection rates of 12 and 6 mg/kg/h.

To estimate the clinical threshold for the anesthesia, we analyzed the distribution and receiver operating characteristic curve of the proposed index (Fig. 6). For the analysis, we integrated the proposed index of all subjects regardless of the injection rate. Given a threshold (Corr = 0.63), we could differentiate the consciousness and unconsciousness with true positive rate (0.91) and false positive rate (0.06).

IV. DISCUSSION

Neurophysiological researches investigate the appearance of decreasing trend in EEG PSD when a subject is unconscious during the GA [18]–[23]. However, the conventional indices have difficulty in quantifying the extent of decreasing trend, since they mostly utilize part of EEG frequency band. To quantify such trend, we newly introduced O-PSD in this paper, and experimentally verified that the O-PSD clearly reveals and quantifies the decreasing trend in EEG PSD of the subjects. By using simple order transformation to the EEG...
PSD, the proposed index achieved a superior distinctiveness of consciousness and unconsciousness, and steadiness during the unconsciousness compared with the conventional indices. Furthermore, the O-PSD is robust to the dynamic range of the EEG PSD.

We demonstrated the efficacy of O-PSD for tens of subjects with single anesthetic, propofol. To prove the generality of O-PSD efficacy, the proposed O-PSD is still needed to be verified for more subjects with different anesthetics such as xenon and ketamine. Also, for the future work, the O-PSD needs to be generalized to utilize multi-channel EEG data. Instead of single channel processing, the spatiotemporal information of the multi-channel EEG O-PSD [29]–[31] with full reflection of the anesthetic characteristics [10] would not only improve the distinctiveness of consciousness and unconsciousness, but also be more robust to the measurement environment or inter-subject dependency. Although we have used the Pearson’s correlation coefficient for measuring the diagonal characteristics of the O-PSD, other deterministic coefficients or machine learning based methods [32], [33] can be applied to quantify the EEG O-PSD.

V. CONCLUSION

We proposed the O-PSD of the EEG PSD to effectively quantify the distinct trend in the EEG spectral power during the GA process. We analyzed the EEG recordings of 15 subjects who were injected with propofol at 12 mg/kg/h, and 12 subjects at 6 mg/kg/h. It was observed that when the subjects were unconscious, clear diagonal pattern appears in the O-PSD. We quantified such spectral trend of O-PSD using Corr, and examined the performance of the proposed index by comparison with conventional indices in terms of the $P_k$, $r_s$, and CV. The experimental results demonstrated that the proposed index is superior in distinguishing consciousness and unconsciousness, and provides a stable and steady measure during unconsciousness. For future work, we briefly discussed about the extension of the anesthetic type, optimizing the method of quantifying the O-PSD pattern, and utilization of multi-channel EEG.

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