ORIGINAL RESEARCH

Characterizing Seizure-Onset Patterns With the Responsive Neurostimulation System

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Purpose: The responsive neurostimulation system (RNS) aims to improve seizures by delivering electrical stimulation in response to epileptiform patterns detected by electrocorticograms. Seizure-onset patterns (SOPs) correspond to outcomes in intracranial EEG (IC-EEG), although whether this is true for RNS is unknown. This study characterizes common RNS SOPs and correlates them with seizure outcomes.

Methods: Among 40 patients with RNS implants, long-episode electrocorticogram characteristics of each patient's seizures were classified by visual analysis as one of the eight patterns previously described in IC-EEG. Correlation between each type of SOP and eventual seizure outcome was analyzed, with $\geq 50\%$ improvement in a number of patient-reported seizure counts defined as a favorable outcome.

Results: Across 263 LEs analyzed, the most common SOP observed was low-voltage fast activity. There was no difference between the distribution of RNS SOPs and that of IC-EEG SOPs described in the literature (Kolmogorov–Smirnov test, $P = 0.98$). Additionally, there was no correlation between any particular SOP and favorable outcomes (Fisher's omnibus test, $P = 0.997$).

Conclusion: This initial description of RNS SOPs finds them to be similar to previously described IC-EEG SOPs, which suggests similar prognostic/therapeutic potential. However, we found that RNS efficacy is independent of patient SOP, suggesting that RNS is likely an equally effective treatment for all SOPs. Future research on stimulation parameters for particular RNS SOPs and correlation with IC-EEG SOPs in the same patients would be instrumental in guiding personalized neurostimulation.

Key Words: Responsive neurostimulation, Seizure-onset pattern, Seizure outcome, Low-voltage fast activity, ECoG.

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The responsive neurostimulation system (RNS) is believed to improve seizures by stimulation of putative epileptogenic zones in response to detected epileptiform activity. The system features two intracranial electrodes that continually monitor electrocorticographic (ECoG) activity. The ECoG data from RNS can contain recordings from both subdural and depth electrodes. When the device detects a seizure-onset pattern (SOP), electrical stimulation is delivered to abort the seizure. The pattern programmed for detection can be tailored according to different parameters including frequency, amplitude, and duration of epileptiform activity.[1]

It is unknown whether these SOPs detected by RNS are similar to those documented during intracranial EEG (IC-EEG) monitoring, which is the current gold standard for detecting epileptiform activity.[2–5] RNS contains two electrodes and a combination of eight contacts that may not always be positioned optimally to detect the true SOP, while IC-EEG monitoring covers a larger density of cortical tissue. Comparing preimplant IC-EEG ECoG patterns with post-RNS SOPs may help ensure that the implant has been positioned optimally.[6] Additionally, while SOPs for IC-EEG have been described in several studies,[2–4,7,8] there is no published work on SOPs for RNS ECoGs to our knowledge, although one abstract is available.[9] With a push toward personalized, data-driven network analysis in neurostimulation for epilepsy, analyzing RNS electrophysiology including SOPs has become increasingly important.[6,10] Hence, we aimed to classify SOPs in RNS to examine whether they correspond to what has been described for IC-EEG.

The methodology used to classify IC-EEG SOPs has varied widely in the literature. At its simplest, seizures have been classified into fast and slow based on traditional EEG frequency bands, where "fast" includes gamma and beta frequency activity and "slow" includes alpha, theta, and delta activity.[7] Another dichotomy described includes the broad categories of hypersynchronous discharges and low-voltage fast activity (LVFA).[8,11] A more granular categorization has been followed by the French and Canadian groups, who have divided SOPs into six,[2] seven,[4] or eight[3] categories. The Marseilles group classified seizure onset into the following eight onset patterns: LVFA (45.6%), preictal spiking followed by LVFA (11.1%), burst of polyspikes followed by LVFA (6.0%), slow wave/DC shift

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followed by LVFA (15.2%), sharp theta/alpha waves (6.7%), beta sharp waves (2.4%), rhythmic spikes/spike-waves (6.7%), and delta-brushes (0.8%).[3] These categories were identified using stereo-electroencephalographic (SEEG) data.[3,4] In our analysis, we followed this classification, which has recently found more acceptance in the literature and between different groups. Lagarde et al.[3] observed that SOP was significantly associated with postsurgical seizure outcomes, with best outcomes for LVFA onset. Another recent study also concluded that preimplant SOPs from IC-EEG can help predict the efficacy of subsequent RNS therapy.[6] However, a comparison of pre- to postimplant SOPs was not performed.

This is an initial description of SOPs commonly seen in RNS ECoG recordings according to the established schema for IC-EEG patterns. Long episodes (LEs) are generally consistent with electrographic seizures.[12] Thus, the objectives of our study were to (1) determine the proportion of LE onsets consisting of particular SOPs in RNS and assess similarity to the IC-EEG distribution in the literature and (2) evaluate the correlation of seizure outcomes with particular SOP.

METHODS

This study was approved by the Institutional Review Board at Baylor College of Medicine. Fifty-eight consecutive patients with preexisting RNS implantations were screened and 40 were included after exclusions (Fig. 1): (1) one patient was deceased and data were not available for review; (2) insufficient seizures: six patients had <5 electrographic seizures available for analysis; (3) short implantation period: four patients had RNS implants <6 months or had stable detection for <3 months; and (4) seven bilateral thalamic implantations were excluded because of potential differences from cortical seizures, although thalamic seizures have been described as a subset of cortical patterns.[5] RNS implantations were performed at Baylor St. Luke's Medical Center between June 2017 and March 2021. Responsive neurostimulation system placement at our institution often follows accurate identification of the epileptogenic zone using IC-EEG.

The RNS stores timestamped raw ECoG data including periodic snapshots of baseline recordings (scheduled ECoG). Detection parameters are programmed within the RNS device. LEs are identified if the detection conditions are met for a predetermined duration, typically 20 seconds or more.[13] The programmed threshold for LE detection in our patients ranged between 9 and 45 s (mean 26.3 seconds, SD 8.3 seconds).

A NeuroPace field engineer (S.C.) initially reviewed the ECoGs for each patient to determine the most common LE and baseline ECoG patterns. Two "baseline" ECoG records containing minimal or no interictal epileptiform activity were selected. After analyzing 100 LEs, five LE patterns' characteristics of each patient's seizures (each ranging from 9 to 45 seconds) were selected by visual analysis as the representative sample for analysis, and the date and time of seizure onsets were recorded. If patients displayed multiple ictal onset patterns, five examples were selected from each onset type. These files were retrieved later and reviewed independently by two board-certified epileptologists (Z.H., J.R.G.) using the patient database management system from Neuropace to characterize the SOPs following the eight IC-EEG patterns characterized by the Marseilles group described above.[3] Visual analysis of the waveforms and spectrogram information within the patient database management system were used for classification; the spectrograms were not made in house. Both ECoGs and spectrograms were available for the same duration, typically 30 seconds prior to the onset and 90 seconds after the onset of the detection. After classifying the SOPs, the two reviewers compared their classifications and resolved any differences by discussion and consensus, following a schema that has been described previously.[2,4] If a majority of the five SOPs were found to be identical, the pattern represented by this majority was assigned as the patient's main SOP. If the sample set was insufficient to classify ictal onset, an additional five representative patterns were identified and classified as described above, for a total of 263 LE ECoGs analyzed across all patients. Pattern A was defined as the patient's main SOP, while Pattern B was defined as the second most common SOP for each patient. Inter-rater reliability was calculated to determine the agreement between the reviewers for both patterns A and B.

The number of seizure occurrences was self-reported by patients during clinic visits via questionnaire. Outcomes were grouped into seven categories: (1) no change, (2) 1% to 24% improvement, (3) 25% to 49% improvement, (4) 50% to 74% improvement, (5) 75% to 89% improvement, (6) 90% to 99% improvement, and (7) seizure free, with ≥50% improvement defined as a favorable outcome. Seizure-onset patterns were categorized as either LVFA or non-LVFA SOPs for analysis to ensure an adequate number of patients per classification because

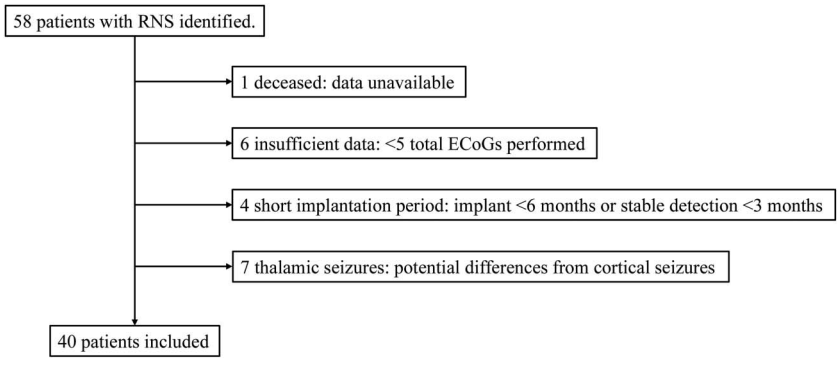

FIG. 1. Flow diagram showing patient inclusion/exclusion criteria for analysis.

some patterns were represented by fewer than five patients. Correlation between favorable seizure outcome and SOP type was evaluated to determine whether RNS efficacy is dependent on SOP.

Statistical Analysis

All data analyses were performed using R statistics version 2023.09.1+494. (R Foundation, Vienna, Austria) with the R Stats package.[14] Pie charts were constructed using Microsoft Excel (Microsoft Inc, Redmond, WA). Inter-rater reliability was calculated using the Cohen's kappa statistic. Similarity between our RNS SOPs and the previously described IC-EEG SOP distribution[3] were assessed using the Kolmogorov–Smirnov goodness-of-fit test. Association of favorable outcomes with LVFA versus non-LVFA SOPs were evaluated using Fisher's exact test.

RESULTS

Among the 40 patients included, hippocampal-onset seizures were observed in 24 (60%). The demographic, seizure-related, and SOP characteristics of included patients are detailed in Table 1. The average age of the patients was 40 years old (SD, 12.6), with an average seizure-onset age of 18 years old (SD, 12.8), which included 24 males and 16 females. Most patients had RNS implants in the hippocampus ($n = 21$). Among the remainder, the implants were in the insula ($n = 3$), temporal lobe ($n = 9$), frontal lobe ($n = 6$), parietal lobe ($n = 2$), or interhemispheric ($n = 3$). MRI showed the mesial temporal lobe involved in 60% ($n = 24$) of patients. The mean follow-up time after RNS implantation was 3.5 (SD, 2.9) years. For each patient, the SOP that occurred most frequently (mode) was identified as the primary SOP type. Representative images of the various SOPs identified, along with the associated spectrogram images, are shown in Fig. 2. The distribution of the various SOPs identified in our study, along with a comparison distribution reported in IC-EEG by Lagarde et al.,[3] is shown in Fig. 3. There was no statistically significant difference found between the two distributions (Kolmogorov–Smirnov test, $P = 0.98$). The overall outcomes of the study population are shown in Fig. 4. The most common pattern was LVFA, comprising 35% ($n = 14$) of our sample, followed by rhythmic slow spikes. The total number of favorable outcomes in our cohort was 72.5% ($n = 29$), of which 11 were in the LVFA group. Of the remaining patients, five had an outcome between 25% and 49%, one patient had an outcome between 1% and 24%, and five patients had no change in their seizure outcomes. No correlation was found between the presence of the LVFA SOP and favorable outcome (Fisher exact test, $P = 0.72$, odds ratio [OR] = 1.61), which suggests that RNS efficacy is independent of SOP. Additionally, no correlation was found between the presence of LVFA SOP and the presence of MTS involvement on MRI (Fisher exact test, $P = 0.50$, OR = 0.54).

A logistic regression was used to analyze the relationship between the SOPs, the presence of MTS versus non-MTS, and sex, on outcomes after RNS implantation and did not show any statistical effects (1) male versus female: OR 1.34, 95% confidence interval (CI) −1.26 to 1.83, $P = 0.71$; (2) LVFA versus non-LVFA SOP: OR 1.44, 95% CI −1.22 to 2.13, $P = 0.66$; and (3) MTS versus non-MTS: OR = 0.27, 95% CI −2.86, 0.14, $P = 0.08$. The inter-rater reliability (Cohen's K) of SOPs at the ECoG level between the reviewers was 0.57 (0.60 for pattern A, 0.40 for pattern B), indicating fair agreement. Inter-rater agreement at the patient level was 0.63 for pattern A (moderate agreement) and 0.19 for pattern B (poor agreement).

DISCUSSION

We investigated the SOPs for LEs detected by RNS in 40 patients with focal epilepsy. Although not statistically significant, the distribution of SOPs in RNS ECoGs differed slightly from that in prior studies of IC-EEG ECoGs. The differences in our interpretation of the findings are described below.

Low-voltage fast activity was found in 35% of our ECoGs, which is lower than seen with IC-EEG (46.5%).[3] This may be because of the higher percentage of mesial temporal lobe epilepsy in our cohort (60%) compared with Lagarde et al., where the mesial temporal onset was reported in only 15% of the sample. The SOP observed in mesial temporal lobe epilepsy is most commonly low-frequency repetitive spiking, while neocortical epilepsy is typically associated with LVFA onsets.[15] Interestingly, unlike our study the majority of the patients included in the Lagarde study had focal cortical dysplasia.[3] We found that there was no correlation between the presence of LVFA SOP and MTS involvement in MRI. Seizure-onset pattern correlation with MTS has not been previously examined in the IC-EEG literature.

Ideally, the RNS electrodes should be implanted as close to the seizure-onset zone as possible. However, there is literature suggesting that less than ideal positioning may control seizures as effectively.[16] Although RNS placement at our institution often follows IC-EEG localization, it is possible that the placement could have missed the predetermined SOZ. As a result, the lack of association between LVFA SOP and favorable outcome may be related to RNS propagation patterns rather than "true SOPs."[2–4] Future studies should investigate the association between seizure outcomes and RNS positioning, along with pre- and post-implant ECoG SOPs.

The proportion of favorable outcome (seizure reduction of 50% or greater) at 3.5 years or more in our patient cohort (75.2%, $n = 29$) is slightly higher than the approximately 65% responder rate at similar time periods in the literature.[16] Another factor to consider is that LEs are not all necessarily electroclinical seizures. LEs are programmatically defined as a set period (typically greater than 20–30 seconds) of a predefined electrographic pattern. As such, there could be a concern that the preprogrammed pattern is likely to be the detected SOP, theoretically leading to a selection bias. In other words, the pattern stored by the ECoG could be dependent on the detection parameters limiting the patterns stored by the device. However, the ranges of detection parameters that are programmed are often broad (e.g., 1–125 Hz), allowing for a wide range of patterns to be detected, and the LEs we found with seemingly similar seizures were sometimes associated with different SOPs.

TABLE 1. Demographic Data With Consensus SOP

Sl. No.	Age	Sex	Electrodes	Age Seizure Onset	MRI	Presurgical IC-EEG Recording Performed	IC-EEG SOZ	RNS Electrode Recording	Number of ECoGs	SOP*	Outcome (%)	Follow-up Duration (Years)
1	51	M	L lat/med hip	40	L lateral temporal lobe encephalomalacia	Subdural	Mesial temporal region	Depth	5	E	25–49	4.56
2	39	M	L hip/R hip	31	Right MTS, B/L PVNH	SEEG	B/L PVNH	Depth	10	A	25–49	3.71
3	28	M	Mid ins/P ins	7	Normal	SEEG	Posterior insula	Depth	5	C	Seizure free	2.96
4	34	M	R hip/R ST	3	Previous left ATLR, R MTS	SEEG	Right mesial hippocampus	Both	5	A	75–89	3.65
5	32	F	L frontal/L PIH	4	Normal	Subdural	L Frontal lobe	strip	5	A	90–99	3.43
6	66	F	L hip/R hip	20	Bilateral MTS	NR	NR	Depth	10	E	50–74	2.66
7	31	M	L hip/R hip	23	Chronic right ACA-MCA watershed infarct	SEEG	B/L mesial temporal region	Depth	10	B	75–89	3.38
8	47	M	L hip/R hip	13	Bilateral MTS	Subdural	B/L mesial temporal region	Depth	10	C	90–99	6.35
9	61	M	L hip/R hip	25	Bilateral MTS	NR	NR	Depth	5	E	75–89	4.40
10	33	M	L hip/R hip	14	Chiari 1 malformation	NR	NR	Depth	5	F	90–99	2.13
11	49	M	L hip/R hip	21	Normal	Subdural	B/L temporal region	Depth	5	C	50–74	4.47
12	26	F	L hip/R hip	21	Cavum vergae cyst	SEEG	Right anterior hippocampus	Depth	5	F	75–89	1.45
13	58	M	L hip/R hip	48	Bilateral mesial temporal sclerosis. Small volume bifrontal encephalomalacia	Subdural	Right temporal region	Depth	5	G	25–49	2.28
14	59	M	L hip/R hip	27	L medial temporal sclerosis	NR	Left temporal region	Both	5	B	75–89	2.08
15	22	F	Sup TP/Inf TP	11	Cortical dysplasia post. Insula, inf. Postcentral and superior/middle temporal	SEEG	Left parietal lobe	strip	5	E	Seizure free	1.13
16	55	F	L hip/R hip	5	L MTS	NR	NR	Depth	5	E	No change	1.30
17	28	F	LAT/L hip	15	Bilateral mesial temporal sclerosis	NR	NR	Both	5	F	1–24	4.11
18	46	M	L hip/R hip	25	Bilateral MTS	Subdural	R/L anterior temporal	Depth	10	A	50–74	5.40
19	43	F	L hip/LAST	38	Left hippocampal inversion	SEEG	L temporal region	Both	5	F	90–99	2.56
20	52	M	L hip/R hip	29	Right temporal encephalomalacia	NR	B/L temporal region	Depth	10	G	Seizure free	7.33
21	23	M	LLT/LLT	11	Cortical tubers and hamartomas	Subdural	L superior temporal region	strip	5	A	Seizure free	4.85
22	42	F	L hip/R hip	25	Cavernous malformation left temporal lobe	SEEG	Anterior hippocampus	Depth	10	G	50–74	1.88
23	42	F	L hip/R hip	30	R more than L MTS	SEEG	B/L temporal region	Depth	10	C	No change	0.85
24	43	F	L hip/R Ins	11	Right open lip schizencephaly and polymicrogyria, with septo-optic dysplasia	SEEG	R insula, R ant temporal lobe, R frontal (schizencephaly)	Depth	5	E	50–74	1.42

(*Continued*)

TABLE 1. (*Continued*)

25	34	M	P1 P2	3	Corpus callosal dysgenesis, colpocephaly. B/L subependymal heterotopia	SEEG	L hippocampus	Depth	5	A	75–89	1.61
26	27	M	L hip/R hip	22	Normal	NR	NR	Depth	10	E	50–74	3.76
27	66	F	L hip/R hip	40	B/L anterior temporal lobes volume loss	NR	NR	Depth	10	A	50–74	2.04
28	31	F	LLT/LLT	3	L parietal encephalomalacia, pineal cyst with mass effect	Subdural	L parieto-occipital convexity	strip	5	A	75–89	5.90
29	49	M	POF/AOF	5	Right MTS, right anterior orbitofrontal resection changes/ encephalomalacia	SEEG	R orbitofrontal region	Depth	5	A	50–74	1.60
30	57	F	Mid Ins/ RTD	3	Changes related to partial right temporal lobectomy and hippocampus resection	SEEG	R temporal lobe and R insula	Depth	5	E	Seizure free	1.13
31	31	M	IFS/PFS	14	Left frontal encephalomalacia	SEEG	L frontal lobe	strip	5	A	90–99	2.85
32	43	M	L hip/R hip	1	Small right PICA territory infarcts	SEEG	B/L hippocampus	Depth	10	E	Seizure free	1.24
33	56	M	LIPF/LIAF	48	Unremarkable	SEEG	L inferior frontal gyrus	strip	5	C	90–99	3.65
34	26	F	L Ins/R Ins	10	Bilateral perisylvian polymicrogyria and abnormal perirolandic sulcation	SEEG	B/L anterior superior insula	Depth	10	A	50–74	1.82
35	48	F	L hip/LST	14	Left MTS, right temporal postsurgical changes. Bifrontal calcifications post-TBI	NR	NR	Both	5	E	25–49	3.19
36	33	M	LD/RD	15	NR	NR	NR	Depth	5	A	75–89	15.46
37	24	M	L FP/L IFS	3	Symmetrically flattened hippocampal heads without signal abnormality	Subdural	L SMA	strip	10	A	25–49	1.97
38	33	M	IFS/SFS	12	Brain volume gliosis and volume loss in left parietal lobe from remote injury	NR	NR	NR	5	A	0	13.44
39	41	M	L hip/R hip	30	Right parietal transmantle sign, without clear cortical dysplasia	SEEG	L hippocampus	Depth	5	E	No change	2.02
40	20	F	LAIH/LPIH	2	Normal	Both	L paracentral lobule	Both	3	E	0	0.93

*Key for SOPs: A, LVFA; B, preictal spiking followed by LVFA; C, burst of polyspikes followed by LVFA; E, rhythmic slow spikes; F, sharp theta/alpha activity; G, beta sharp activity.

ACA-MCA, anterior cerebral artery-middle cerebral artery; AOF, anterior orbitofrontal; AT, anterior temporal strip; ATLR, anterior temporal lobe resection; BL, bilateral; F, female; FP, frontoparietal; hip, hippocampus; IFS, inferior frontal strip; Inf, inferior; ins, insula; L, left; LAIH, left anterior interhemispheric; LAST, left anterior subtemporal; LAT, left anteriotemporal; LD, left (mesial temporal) depth; LIAF, left inferior anterior frontal strip; LIPF, left inferior posterior frontal strip; LLT, left lateral temporal strip; LPIH, left posterior interhemispheric; LST, left subtemporal; M, male; MTS, mesial temporal sclerosis; N/A, not applicable; NR, not reported; P, posterior; P1, superior parietal lobule; P2, inferior parietal lobule; PFS, posterior frontal strip; PICA, posterior inferior cerebellar artery; PIH, posterior interhemispheric; POF, posterior orbitofrontal; PVNH, periventricular nodular heterotopia; R, right; RD, right (mesial temporal) depth; RTD, right temporal depth; SEEG, stereoelectroencephalography; SFS, superior frontal strip; SOP, seizure-onset pattern; Sup, superior; TBI, traumatic brain injury.

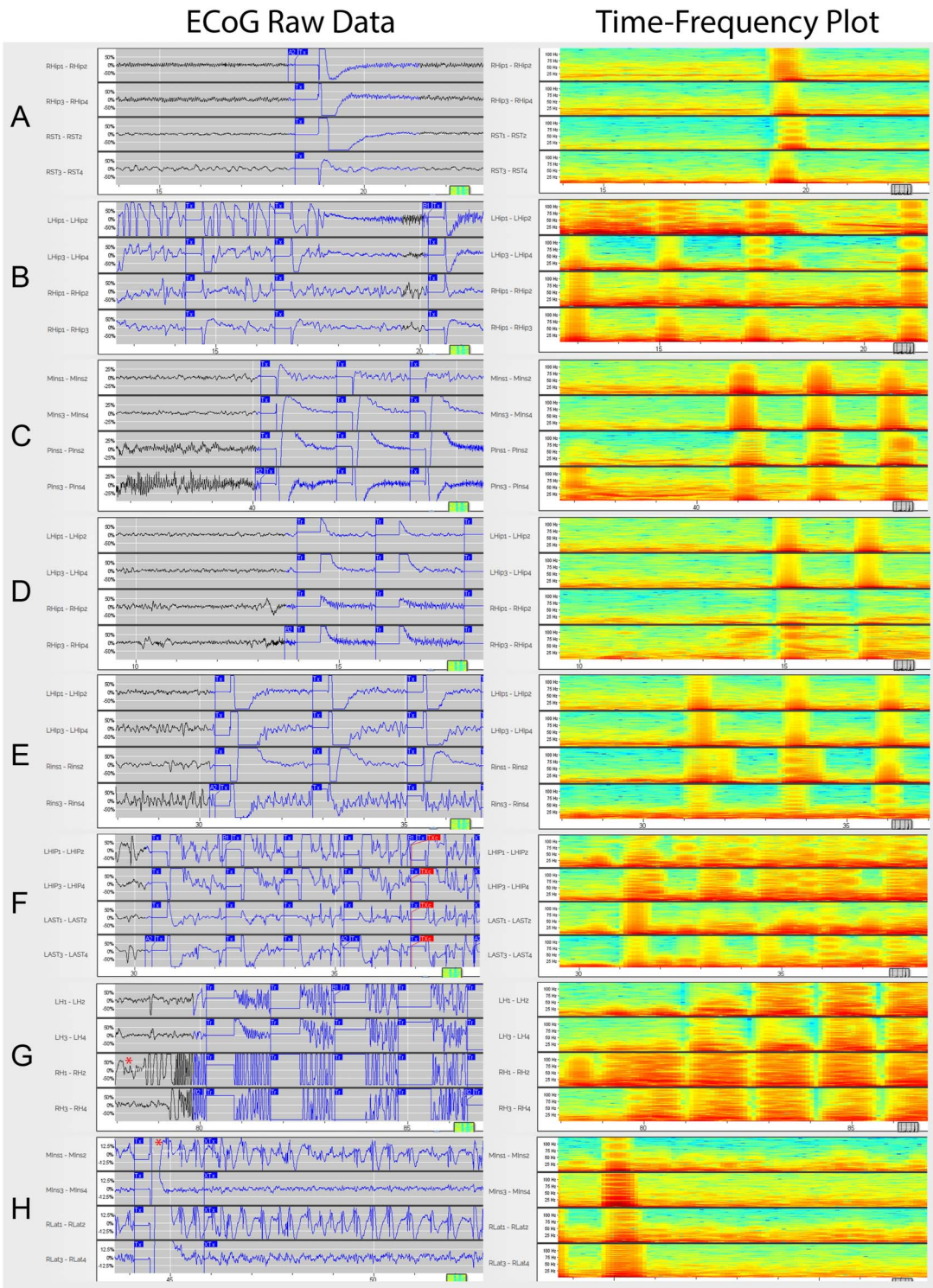

FIG. 2. Representative images of various SOPs. **A**, LVFA. **B**, Preictal spiking followed by LVFA. **C**, Burst of polyspikes followed by LVFA. **D**, Slow wave or baseline shift followed by LVFA. **E**, Rhythmic slow spikes. **F**, Sharp theta/alpha activity. **G**, Beta sharp activity. **H**, Delta brush. Red asterisks mark seizure onset. The time–frequency plot (spectrogram) colors represent "heat maps" with red colors, indicating higher incidence of particular frequencies (shown in *y*-axis) at particular timepoints (*b*-axis). EEG frequencies are shown between 1 and 125 Hz (sampling frequency 250 Hz). LVFA, low-voltage fast activity; SOP, seizure-onset pattern.

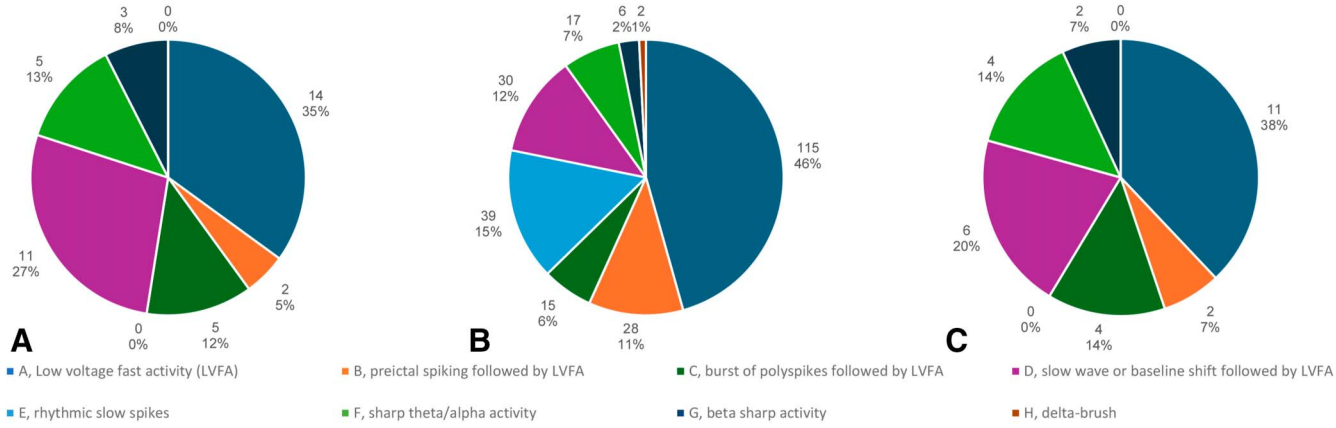

FIG. 3. Pie charts showing distribution of seizure-onset patterns for individual seizures (**A**) compared with distribution reported in the literature[3] (**B**), as well as distribution of seizure-onset patterns among patients with favorable outcomes (**C**).

This suggests that RNS may not necessarily favor the preprogrammed pattern automatically but is rather able to detect a variety of SOPs even with subtle differences. Although there is no way of knowing whether patterns not stored were even more diverse, the diversity seen in our recordings appears to reduce the likelihood of this limitation. Additionally, because the ECoG stored by RNS will include 30 seconds before the detector onset, we were able to look back and examine whether the actual seizure onsets had a different SOP. Another way of minimizing the effect of preset pattern detection is to analyze the seizures detected by line length before the bandpass filters are initiated, although this method was not used in our study. Line length detectors are a measure of power that compares the ECoG length in a short time period (typically 1–4 seconds) to that in a long-term window (typically 1–2 minutes). The detector is activated when the difference between the short-term and long-term trend windows exceeds a programmed threshold.[17] The inter-rater agreement was moderate; however, this is consistent with prior studies of IC-EEG SOPs.[4] LEs were initially screened for review by prescreening thumbnails in the patient database management system. Two reviewers independently examined the SOPs and discussed them to reach a consensus, following a scheme that has been described previously.[2,4] This may have affected the detection of SOPs during review. However, this process also provided for a more quantitative review in determining the most commonly identified SOP for a given patient. Most patients had one main pattern identified, while others had a second SOP that was less consistently seen and, therefore, less homogeneous as evidenced by the lower inter-rater reliability for pattern B. This is contrary to prior literature, which looked at one representative seizure for each patient.[4]

Long episodes were visually examined to ensure that these were electrographic seizures based on evolution, although

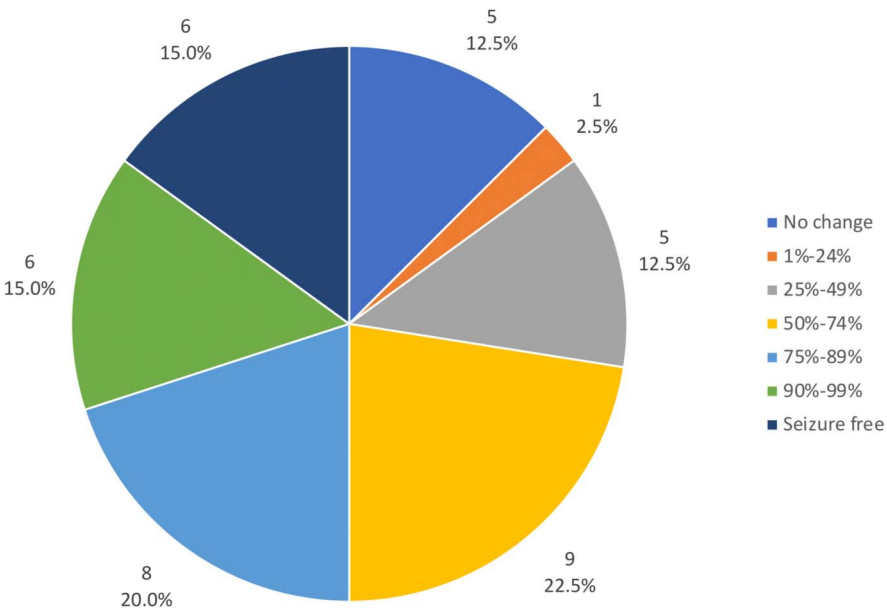

FIG. 4. Pie chart showing distribution of best seizure outcomes of responsive neurostimulation system treatment by percent improvement.

retrospective correlation with clinical seizures was not feasible for these events in the distant past. Magnet swipes were also present in only a small percentage of the seizures. We were not averse to examining SOPs of potentially subclinical (electrographic) seizures that could have happened without the patient's awareness or in sleep because the research focus was in identifying SOPs of all seizures, not just clinically recognized seizures.

Our workflow was also influenced by another limitation—as opposed to traditional IC-EEG review, we were unable to manipulate the filter settings and notch filters when reviewing RNS LEs. IC-EEG SOPs are typically examined without filtering and have the option of adaptable filters to aid in identifying certain bandwidths, whereas the RNS system is documented to have high- and low-pass filters that are not adjustable.[18] This limited our ability to evaluate the visible patterns, and we supplemented this with a review of the spectrogram to determine the underlying frequency distributions. Region-specific features of SOPs, such as lowered amplitude for LEs captured in the insula, also required a review on a 2x gain. Additionally, while Lagarde et al. used SEEG data and generated time–frequency analysis of their recordings, we were restricted to the ECoG and spectrograms provided within the patient database management system.

Furthermore, several LEs had patterns that defied the preexisting classification scheme used in the literature. This most commonly manifested as a repetitive spiking pattern that was slower than the 6- to 14-Hz rhythmic slowing spikes described in the Lagarde classification. Further characterization of RNS SOPs is required to better clarify whether the modification of the preexisting classification scheme is necessary. It is yet unclear whether the patterns commonly described for IC-EEG are those that would be most applicable for RNS or whether there should be a different classification scheme for RNS. Lagarde et al. used sampling rates of 256, 512, and 1,024 Hz. While the sampling rates of the RNS system are toward the lower end of the range at 250 Hz,[18] it should not lead to practical differences because the fastest analyzed rhythms of LVFA were in the range of 15 to 30 Hz and would have been easily visualized with the sampling frequency of the RNS system.

Another limitation of the study is that the effect of antiseizure medication adjustments was not accounted for. While standard practice at our institution is to minimize medication adjustments soon after RNS implantation, some adjustments were likely made, which could have affected the outcomes. Variables such as the number of changes, timing of changes, and outcomes would be too heterogeneous to effectively analyze subgroup outcomes. Another limitation was that we did not examine the number of daily RNS therapies for its correlation with seizure outcomes. This is an initial description of SOPs commonly seen in RNS ECoG recordings according to the established schema for IC-EEG patterns. Because neurostimulation treatment for epilepsy becomes increasingly data-driven and personalized, analyzing and characterizing RNS electrophysiology is ever more valuable.[10] In this study, we found that the distribution of SOPs detected by RNS is statistically similar to that detected by IC-EEG, the current gold standard ($P = 0.98$)—this comparison suggests a similar prognostic/therapeutic potential. We also found that RNS efficacy is independent of patient SOP, meaning that RNS is likely an equally effective treatment for all SOPs. Our findings may guide further research on RNS SOPs, which could help continue to explore the impact of SOP type on RNS outcomes. A recent proof-of-concept study showed the value of pre-RNS IC-EEG recording in predicting RNS outcomes, where IC-EEG synchronicity was able to differentiate responders from nonresponders of RNS.[6] Further research could include comparing patients' own IC-EEG ECoGs to their RNS ECoGs to verify positioning and confirm that the detector is appropriately programmed to detect the SOP. Additionally, specific SOPs may be more responsive to certain RNS stimulation parameters; therefore, further studies on these parameters for particular RNS SOPs and their correlation with IC-EEG SOPs in the same patients would be instrumental in guiding the evolution of personalized neurostimulation.

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