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Systematic review of seizure-onset patterns in stereo-electroencephalography: Current state and future directions

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HIGHLIGHTS

- The most prevalent seizure-onset patterns (SOPs) are low frequency periodic spikes (LFPS) and low-voltage fast activity (LVFA).
- LFPS had the most divergent terminology, whereas LVFA had the most reproducible terminology.
- Some SOP terms were inconsistent with standard EEG terminology.

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ABSTRACT

Objective: Increasing evidence suggests that the seizure-onset pattern (SOP) in stereo-electroencephalography (SEEG) is important for localizing the "true" seizure onset. Specifically, SOPs with low-voltage fast activity (LVFA) are associated with seizure-free outcome (Engel I). However, several classifications and various terms corresponding to the same pattern have been reported, challenging its use in clinical practice.
Method: Following the Preferred Reporting Items of Systematic reviews and Meta-Analyses (PRISMA) guideline, we performed a systematic review of studies describing SOPs along with accompanying figures depicting the reported SOP in SEEG.
Results: Of 1799 studies, 22 met the selection criteria. Among the various SOPs, we observed that the terminology for low frequency periodic spikes exhibited the most variability, whereas LVFA is the most frequently used term of this pattern. Some SOP terms were inconsistent with standard EEG terminology. Finally, there was a significant but weak association between presence of LVFA and seizure-free outcome.
Conclusion: Divergent terms were used to describe the same SOPs and some of these terms showed inconsistencies with the standard EEG terminology. Additionally, our results confirmed the link between patterns with LVFA and seizure-free outcomes. However, this association was not strong.
Significance: These results underline the need for standardization of SEEG terminology.

1. Introduction

Surgical treatment is the only potentially curative treatment in patients with drug-resistant focal epilepsy, provided that the complete epileptogenic zone (EZ) is resected (Rosenow and Lüders, 2001). However, prior to the surgery, a precise delineation of the presumed EZ is needed; invasive electro-encephalography (EEG) monitoring is required in up to 30% of the patients to define this area (Rugg-Gunn et al., 2020).

One of the main features considered by clinicians when analyzing intracranial EEG is the seizure onset pattern (SOP). Numerous studies have reported a correlation between the SOP and surgical

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outcomes (Lagarde et al., 2019a; Singh et al., 2015). Patients exhibiting a SOP involving low-voltage fast activity (LVFA) are more likely to achieve seizure freedom after surgery than those without LVFA. However, heterogeneous terminology and multiple classifications from various epilepsy centers around the world have been used in previously published studies (Cui et al., 2022; Doležalová et al., 2013; Feng et al., 2020; Di Giacomo et al., 2019; Gnatkovsky et al., 2019; Lagarde et al., 2016; Michalak et al., 2023; Perucca et al., 2014). Notably, several SOPs have been reported using divergent terms while representing almost the same electrical pattern. Moreover, the range of SOPs varies from one to nine and the type of SOPs also vary even within studies that have examined a wide range of epilepsy types (Lagarde et al., 2019a; Perucca et al., 2014). Clearly, a single SOP is inadequate to encompass the diverse SOPs across the entire spectrum of epilepsies, whereas nine patterns may be redundant and add unnecessary complexity when integrating them into clinical practice.

Invasive EEG serves as the gold standard for delineating the presumed EZ in cases with more complex epilepsy (McGonigal et al., 2007). This can be achieved through either subdural grids/strips or stereo-electroencephalography (SEEG), which consists of inserting intracerebral electrodes via a stereotactic framework. Even though both techniques invasively record neuronal activity, they exhibit fundamental differences that lie primarily in the placement of electrodes (atop the cortex vs. intracerebral) and the depth of brain regions they record from (Gonzalez-Martinez et al., 2013; Jehi et al., 2021; Minotti et al., 2018). Grids/strips are indeed positioned on the cortical surface, offering high-resolution surface recordings from the gyral crowns, while SEEG involves depth electrodes that penetrate deeper brain structures like the amygdala, hippocampus, and areas where focal cortical dysplasia (FCD) type II is often found (bottom of sulcus) (Chassoux et al., 2012; Jehi et al., 2021; Roca et al., 2015). These fundamental differences account for differences in EEG presentation of SOPs between the two modalities. Furthermore, considering the higher tolerance and the fewer side-effects of SEEG when compared to grids/strips (Jehi et al., 2021; Yan et al., 2019), there is an increasing global utilization of the SEEG technique in the presurgical work-up of drug-resistant epilepsy (Abou-Al-Shaar et al., 2018). Therefore, it is important to separately investigate the SEEG SOPs.

Only few systematic reviews on this subject have been published (Shakhatreh et al., 2022; Singh et al., 2015). One of these reviews is a nearly decade-old systematic review and *meta*-analysis (Singh et al., 2015), while the other is centered around malformations of cortical development (Shakhatreh et al., 2022). Notably, neither of these reviews addressed specifically the challenges of the heterogeneous terminology. Furthermore, both systematic reviews considered intracranial EEG SOPs as a unified entity without separating SOPs recorded with grids/strips from those with SEEG.

To address this clinically important gap, (i) we conducted a systematic literature review focused on SOPs in SEEG, (ii) we highlighted the heterogeneity in terminology, (iii) we performed a comparison to standard EEG terminology, and (iv) we performed a *meta*-analysis to assess the relationship between SOPs with and without LVFA and surgical outcomes.

2. Methods

The study protocol was registered on the international prospective register of systematic reviews (PROSPERO; number CRD42023458503) and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Page et al., 2021).

2.1. Review questions

The aims of this review were to (i) evaluate the variability in the terminology of SOPs by identifying identical EEG patterns referred to under different terminologies, (ii) group them under a unified terminology in SEEG recordings, (iii) compare the SEEG SOP definitions with the definitions broadly used in clinical EEG (Kane et al., 2017), and (iv) based on previous reports about the relationship between LVFA-associated SOPs and surgical outcome, we formulated our review question using the Participants, Intervention, Comparison, Outcome, Study design (PICOS) framework as follows: "Do SOPs with LVFA result in better surgical outcome when compared to those without LVFA?" In this context, we considered: P: patients with drug-resistant epilepsy who underwent SEEG investigation as part of their presurgical evaluation; I: the interventions included open epilepsy surgery, thermocoagulation, or laser ablation, with a follow-up duration of at least one year post-surgery; C: the comparison entailed distinguishing between the group of patients with LVFA-associated SOPs and those without; O: the outcome of interest was the surgical outcome; and S: this systematic review included both prospective and retrospective studies that reported SOPs recorded during SEEG investigation. Additionally, for the review question, we included studies that conducted a comparison between surgical outcome and SOPs.

2.2. Literature search strategy

We systematically searched electronic databases (PubMed and Web of sciences all databases) to identify articles that reported SOPs during SEEG investigation. Relevant key terms related to SOP and SEEG in combination as MeSH terms such as "seizure-onset pattern", or "ictal onset pattern", or "seizure pattern", or 'ictal pattern", or "*peri*-ictal spiking" or "limbic spiking" and "stereoelectroencephalography", or "SEEG", or" intracranial EEG", or "stereo-electro-encephalography" were used across the two databases up to 04/17/2023 (see details in Supplementary Material 1).

2.3. Inclusion and exclusion criteria

We included studies reporting at least 10 patients who underwent SEEG recordings as part of their presurgical investigation, with a clear description of the SOP with available figures for each reported SOP. We excluded studies not reported in English language, review articles as they did not contain primary data, conference abstracts, non-peer reviewed papers, or studies with grids/strips except in mesio-temporal cases when depth electrodes targeting the mesio-temporal structures were implanted. Lastly, studies lacking a clear description of the SOP (or references for the described EEG patterns) and without illustrative examples were excluded.

2.4. Study selection, data extraction

The selection process for papers meeting the inclusion criteria comprised two stages. Initially, a primary reviewer (CA) examined the titles and abstracts of all studies identified by the selection criteria to identify eligible papers. Eligible papers were defined as those meeting some of the inclusion criteria at this stage, specifically papers that pertained to seizure patterns during SEEG or intracranial EEG, with a minimum of 10 patients. In cases where the title or abstract of an article only referred to intracranial EEG, the paper was considered eligible.

After this initial screening phase, all duplicate articles were removed, and the eligible studies proceeded to full-text screening. The full-text screening was performed independently by two

authors (CA and DM). Disagreements were resolved through consensus between the two reviewers. For each eligible article, we extracted pertinent details including the title, first author, journal of publication, publication year, cohort size, names and number of SOPs, population type (adult, children, mixed cohort), and the type of intracranial EEG investigation employed (SEEG, a combination of grids/strips and depth electrodes). Additionally, for manuscripts satisfying all inclusion criteria, we extracted SOP definitions as reported by the authors, along with corresponding figures, the country where the study was conducted, and the epilepsy type of the studied cohort (e.g., mesio-temporal cases, negative MRI, post-traumatic).

Lastly, for studies investigating the association between SOPs and surgical outcome with at least one year of postoperative follow-up, we extracted tables containing demographic information, such as patient age, sex, age at epilepsy onset (if available), the number of operated patients, the number of seizure-free patients postoperatively, and the number of non-seizure-free patients for subsequent statistical analysis.

2.5. Quality assessment

To assess the risk of bias in the included studies, one author (CA) applied the criteria previously outlined by Singh et al. (2015). These criteria encompassed the following aspects: (1) EEG interpretation conducted by more than one independent reader; (2) blinding of EEG readers to diagnosis and outcome; (3) interpretation requiring agreement between EEG readers; (4) inclusion of consecutive patients; and (5) comprehensive inclusion of all patients in the analysis. The assessment employed a maximum score of 5, with higher scores indicating superior study quality.

2.6. SOP terminology

To facilitate meaningful comparisons of the diverse SOPs, which are often described using a wide range of terminologies in the existing literature, our initial approach involved identifying identical EEG patterns referred to under different terminologies and referring to them under a unified terminology. To achieve this, we prioritized the most frequently utilized term found in the literature, selecting terms that comprehensively encompass or correspond to other descriptions based on various EEG attributes, such as frequency, amplitude, and duration. Furthermore, we proposed a definition for each SOP based on the terminology, which was most frequently used in the literature. Subsequently, we listed all reported SOPs, consisting of 14 distinct patterns. Additionally, we highlighted discrepancies between the terms used in the SEEG literature and their definition broadly used in clinical EEG, according to the EEG Glossary of the International Federation of Clinical Neurophysiology (IFCN) (Kane et al., 2017). Finally, to allow a smooth implementation into clinical practice, we streamlined these groups further into two archetypical patterns, based on the presence or absence of LVFA (SOPs with LVFA and SOPs without LVFA). We argue, that although 14 categories may appear to provide a more accurate description, the lack of clinical significance between patterns makes their distinction irrelevant, increases the confusion in this field and makes collaborative research more difficult.

2.7. SOPs vs. outcome, epilepsy topography, and etiology

Most studies assessing the relationship between SOPs and surgical outcome found that certain patterns are more likely to be associated with seizure-freedom postoperatively compared to others (Lagarde et al., 2019a, 2016; Singh et al., 2015). After listing the 14 SOPs, we dichotomously grouped them into SOPs with LVFA and SOPs without LVFA, hypothesizing that the former are associated with better outcome.

In addition to studying the correlation between SOPs and surgical outcome, we investigated their relationships with epilepsy topography and etiology (epileptogenic lesion on the MRI/after pathological examination). Knowing that certain patterns are associated with mesio-temporal lobe epilepsy (mTLE) and others with neocortical generators (Singh et al., 2015), we classified patients into mTLE versus extra- mTLE. Similarly, considering the prevalence of specific patterns in malformation of cortical development (MCD) (Lagarde et al., 2019a) and others in hippocampal sclerosis (HS) (Frauscher et al., 2017; Singh et al., 2015), we categorized patients into HS versus other etiologies, and MCD versus other etiologies. For mTLE and HS realated-analysis, we grouped the 14 SOPs into the three main reported SOPs in this category (Feng et al., 2020; Ilyas et al., 2022) (low-frequency periodic spikes (LFPS), LVFA-SOPs and others). For MCD versus others, we grouped the 14 SOPs into four categories (LFPS, LVFA-SOPs, burst of polyspikes, other-SOPs).

2.8. Data synthesis and analysis

We conducted a *meta*-analysis of the postsurgical outcome after resection of SOPs with LVFA vs. without LVFA. We extracted data from all studies reporting the relationship between SOPs and surgical outcome, with a follow-up duration of at least one year, alongside available tables or figures outlining SOP types. Surgical outcome encompassed patients undergoing open, resective brain surgery, thermocoagulation, or laser amygdalohippocampectomy. In cases where multiple studies met these criteria but originated from a single center, only the study with the largest patient cohort was considered for analysis to prevent biases associated with overrepresentation of a single dataset and re-use of the same patients in different studies. We classified patients into seizure-free (Engel I) and non-seizure-free (Engel II-IV) surgical outcome by using the Engel classification (Engel et al., 1993). We used the Chi-square test for statistical analysis. The effect size was computed using the Phi coefficient. Similarly, we investigated the associations between SOP and epilepsy topography, and between SOP and etiology. We used a Chi-squared goodness of fit test to examine potential differences in the distribution of categorized SOPs across epilepsy topography types and etiology types. A $p \leq 0.05$ was considered statistically significant. Statistical tests were performed in Microsoft Excel.

3. Results

3.1. Study selection

The database search yielded 1799 studies, of which 61 were potentially eligible. Following the full-text screening process, a total of 22 studies met the inclusion criteria, as shown in the PRISMA flow diagram (Fig. 1). Notably, discrepancies in the inclusion were found only in 4 out of 61 (6%) studies by the two independent reviewers. All but one of the included publications had a retrospective design (Ilyas et al., 2022), and were published between 2000 and 2022. Most of these studies (17 out of 22, 77%) assessed SOPs within a mixed cohort encompassing both children and adults. Five publications were from Canada (Ferrari-Marinho et al., 2016; Frauscher et al., 2017; Makaram et al., 2020; Perucca et al., 2014; Tanaka et al., 2018), six from France (Bartolomei et al., 2005; Chassoux et al., 2000; Fierain et al., 2020; Lagarde et al., 2019a, 2019b, 2016), five from the USA

(Ilyas et al., 2022; Michalak et al., 2023; Schuh et al., 2000; Steriade et al., 2020; Velasco et al., 2000), three from China (Cui et al., 2022; Feng et al., 2020; Liu et al., 2021), two from Italy (Di Giacomo et al., 2019; Gnatkovsky et al., 2019), and one from the Czech Republic (Doležalová et al., 2013). The total number of patients was 1146 (range: 11–252 patients)), while the total number of reported seizures was 4057 (range: 30–820). A summary of the included studies is shown in Table 1.

3.2. Quality assessment

On the quality score scale of 5 (with higher values indicating better quality), 11 studies (Cui et al., 2022; Feng et al., 2020; Ferrari-Marinho et al., 2016; Fierain et al., 2020; Lagarde et al., 2019a, 2019b, 2016; Makaram et al., 2020; Michalak et al., 2023; Perucca et al., 2014; Tanaka et al., 2018) (50%) reached a score of 5, 3 studies (Di Giacomo et al., 2019; Gnatkovsky et al., 2019; Steriade et al., 2020) (14%) were considered having a score of 4, 5 studies (Bartolomei et al., 2005; Doležalová et al., 2013; Frauscher et al., 2017; Schuh et al., 2000; Velasco et al., 2000) (22%) 3, and 3 studies (Chassoux et al., 2000, 2000; Ilyas et al., 2022; Liu et al., 2021) (14%) 2.

3.3. Definition of the SOPs

Generically, the SOP was defined in most studies as the first change of the SEEG signal within the context of a sustained rhythmic discharge, followed by the emergence of clinical manifestations (Bartolomei et al., 2005; Cui et al., 2022; Feng et al., 2020; Fierain et al., 2020; Lagarde et al., 2019a, 2016; Makaram et al., 2020; Perucca et al., 2014; Tanaka et al., 2018) Consequently, these studies excluded seizures where clinical manifestations preceded the ictal EEG changes. Definition of the SOPs in the included papers are detailed in Supplementary Material 2.

To allow a meaningful comparison among all SOPs documented in the literature and to consolidate those with divergent terminologies yet representing the same EEG pattern, we grouped all published SOPs into 14 distinct categories. In other words, we considered synonyms which refer to the same EEG pattern, and we listed them under a unified equivalent term. Among these, the most frequently reported SOP were LFPS and LVFA both identified in 20/22 (91%) studies, followed by sharp activity (rhythmic theta/alpha activity) in 16 studies (73%). Conversely, the least frequently described SOP was a mixed pattern, present in only a single study dedicated to post-encephalitic epilepsies (Steriade et al.,

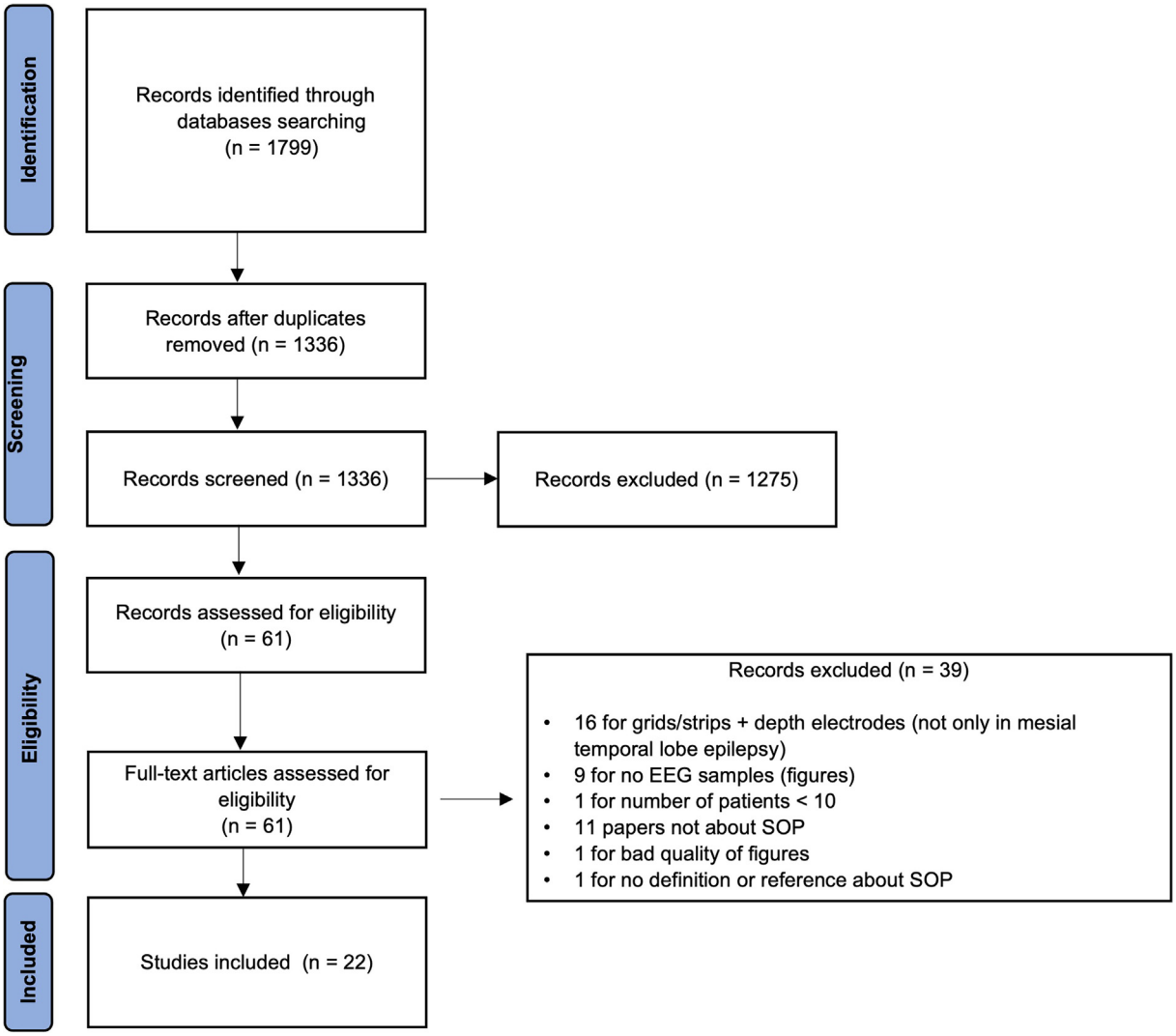


Fig. 1. Flow diagram following the PRISMA guidelines.

Table 1
Summary of the 22 included studies.

Study	Journal of publication	Country	Design	Number of SOPs	Number of patients	Population (Years of age)	Quality	Epilepsy topography	Surgical outcome
Velasco et al., 2000	Neural Plasticity	USA	Retrospective	2	68	Mixed (15–49)	3	MTLE	No
Schuh et al., 2000	Epilepsia	USA	Retrospective	1	40	Not reported	3	MTLE	Yes
Chassoux et al., 2000	Brain	France	Retrospective	2	28	Mixed (5–41)	2	Multiple	No*
Bartolomei et al., 2005	Epilepsia	France	Retrospective	2	11	Mixed (14–43)	3	MTLE	No
(Doležalová et al., 2013)	Clinical Neurophysiology	Czech Republic	Retrospective	3	51	Mixed (13–54)	3	TLE	Yes
Perucca et al., 2014	Brain	Canada	Retrospective	7	33	Mixed (16–54)	5	Multiple	Yes (Supplementary Material)
Lagarde et al., 2016	Epilepsia	France	Retrospective	6	53	Mixed (2.75–56)	5	Multiple	Yes
Ferrari-Marinho et al., 2016	Epilepsy Research	Canada	Retrospective	6	37	Mixed (16–56)	5	Multiple	No
Frauscher et al., 2017	Clinical Neurophysiology	Canada	Retrospective	2	18	Adult (36.7 ± 12.1)	3	MTLE	No
Tanaka et al., 2018	Epilepsia	Canada	Retrospective	7	61	Mixed (16–60)	5	Multiple	No
Gnatkovsky et al., 2019	Epilepsia	Italy	Retrospective	4 (2 main SOPs)	105	Mixed (3- 50)	4	Multiple	No*
Lagarde et al., 2019a	Epilepsia	France	Retrospective	8	252	Mixed (26.3 +/- 13.8)	5	Multiple	Yes
Di Giacomo et al., 2019	Seizure	Italy	Retrospective	5	102	Mixed (26.6 ± 12)	4	Multiple	Yes
Lagarde et al., 2019b	Journal of Neurology	France	Retrospective	7	59	Adult (30.4 ± 12)	5	Multiple	Yes
Feng et al., 2020	Clinical Neurophysiology	China	Retrospective	5	28	Mixed (15–60)	5	MTLE	No*
Makaram et al., 2020	Clinical Neurophysiology	Canada	Retrospective	5	24	Not reported	5	Multiple	No
Fierain et al., 2020	Epilepsy & Behavior	France	Retrospective	8	18	Adult (25–61)	5	Multiple	No*
Steriade et al., 2020	Clinical Neurophysiology	USA	Retrospective	4	17	Mixed (6–59)	4	Multiple	No*
Liu et al., 2021	Epilepsy & Behavior	China	Retrospective	2	27	Mixed (3–46)	2	Other	Yes (thermo-coagulation)
Ilyas et al., 2022	Clinical Neurophysiology	USA	Prospective	3	11	Adult (23–59)	2	MTLE	Yes
Cui et al., 2022	Acta Neurochirurgica	China	Retrospective	5	45	Mixed (6–45)	5	TLE	Yes
Michalak et al., 2023	Epilepsia	USA	Retrospective	9 (+ED)	58	Adult (20–66)	5	MTLE	Yes (SLAH)

MTLE: mesio-temporal lobe epilepsy; TLE: temporal lobe epilepsy; SLAH: stereo-electroencephalography-guided laser amygdalohippocampotomy; ED: electrodecrement; No*: surgical outcome reported, but not directly in relation with the different SOPs, Other: Hypothalamic hamartoma, Multiple: TLE and extra TLE.

2020). Additionally, delta activity, burst-suppression, and electrodecrement patterns were each observed in only 2 studies (9%).

Across the diverse definitions involving the three most prevalent SOPs, we found that LFPS (Fig. 2) was commonly defined as low-frequency, high-amplitude spikes with a frequency below 2 Hz and a duration exceeding 5 s. LVFA (Fig. 3) was often identified as low-voltage (<10 μV), high-frequency (>13 Hz) activity. Sharp activity (rhythmic theta/alpha activity; Fig. 4), on the other hand, was typically defined as contoured rhythmic activity with a frequency $\leq$ 13 Hz.

Among the diverse SOP terms, we found that LFPS exhibited the highest degree of variability in its terminology (preictal spiking, ictal spiking, hypersynchronized spikes, low frequency repetitive spiking, repetitive spiking, low frequency high amplitude periodic spikes, low frequency high amplitude rhythmic spikes, periodic spiking, slow burst, or slow rhythmic spikes). In contrast, LVFA demonstrated a notable consistency in its terminology, being reported under the same name (term) in nearly all studies (17/20 studies; in one study, it was denoted as tonic discharge (Bartolomei et al., 2005), in another as fast ictal activity (Doležalová et al., 2013), and in the last one as low amplitude fast activity (Ilyas et al., 2022)).

3.4. Definition of SOPs and standard EEG terminology

For three of the 14 SOPs, we found inconsistencies between the SEEG terms used in the literature and their definition broadly used in clinical EEG (Fig. 5): burst of polyspikes, burst-suppression and delta-brush (Kane et al., 2017). In SEEG, the burst of polyspike SOP was often defined as polyspikes of high frequency and amplitude and short duration (<5 s) followed by LVFA (Fig. 6); indeed, in the IFCN EEG glossary, the term burst is not a synonym of paroxysm. Precisely, a burst is defined as a group of waves with a minimum of four phases and duration longer than 500 ms which appear and disappear abruptly and are distinguished from background activity by differences in frequency, form and/or amplitude (Kane et al., 2017). The appearance and disappearance characteristic is lacking in the reported SEEG examples (Fig. 6). Similar differences are noted for the SEEG burst-suppression SOP and the SEEG delta brush SOP pattern. Definitions of both patterns deviate from the EEG glossary. In standard EEG terminology, burst suppression is defined as paroxysmal bursts of theta and/or delta waves, at times intermixed with sharp and faster waves, alternating with intervening periods of attenuation/suppression lasting more than 50% of the recording; delta brush is defined as either a normal neonatal grapho-element or a combination of delta wave with superimposed fast activity >8 Hz (Kane et al., 2017).

3.5. SOPs with vs. without LVFA

Previous studies suggested that the presence of LVFA was associated with a better outcome compared with SOPs without LVFA (Ilyas et al., 2022; Lagarde et al., 2019a, 2016; Liu et al., 2021; Michalak et al., 2023; Schuh et al., 2000; Singh et al., 2015). Given

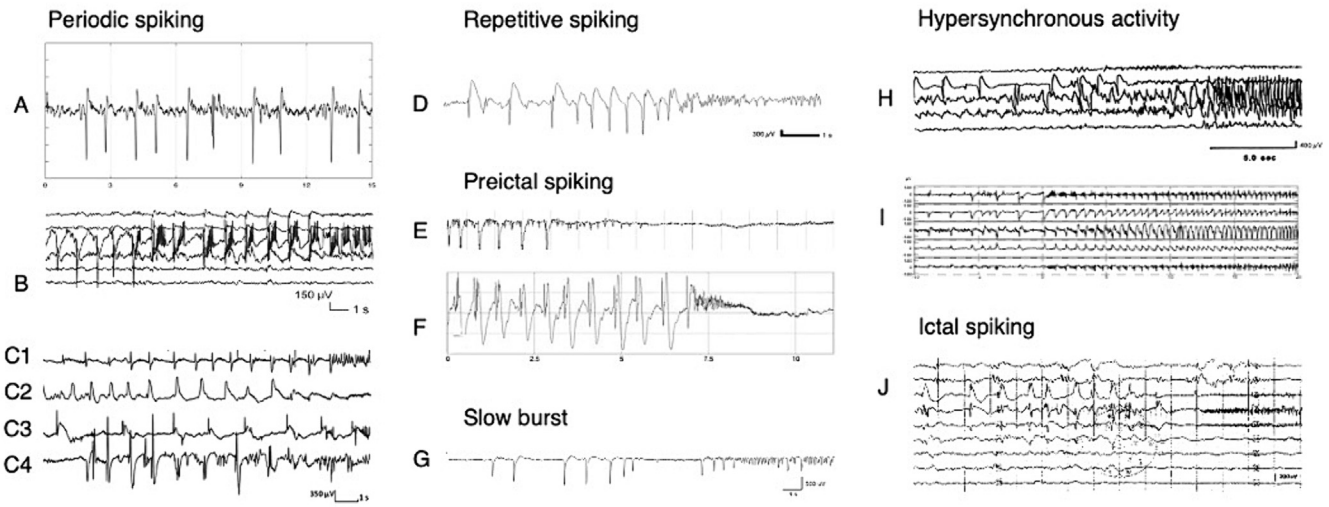


Fig. 2. Depicts divergent terminologies of LFPS across numerous studies: low-frequency periodic spiking in A (Cui et al., 2022), B (Perucca et al., 2014), and C (Frauscher et al., 2017); low-frequency repetitive spiking in D (Michalak et al., 2023); Preictal spiking in E (Fierain et al., 2020); Preictal spiking with rhythmic spikes of low frequency in F (Lagarde et al., 2016); slow burst of polyspikes in G (Di Giacomo et al., 2019); Hypersynchronous activity in H (Velasco et al., 2000) and I (Ilyas et al., 2022); and repetitive ~1-Hz spike discharges in J (Schuh et al., 2000). LFPS: low-frequency periodic spikes.

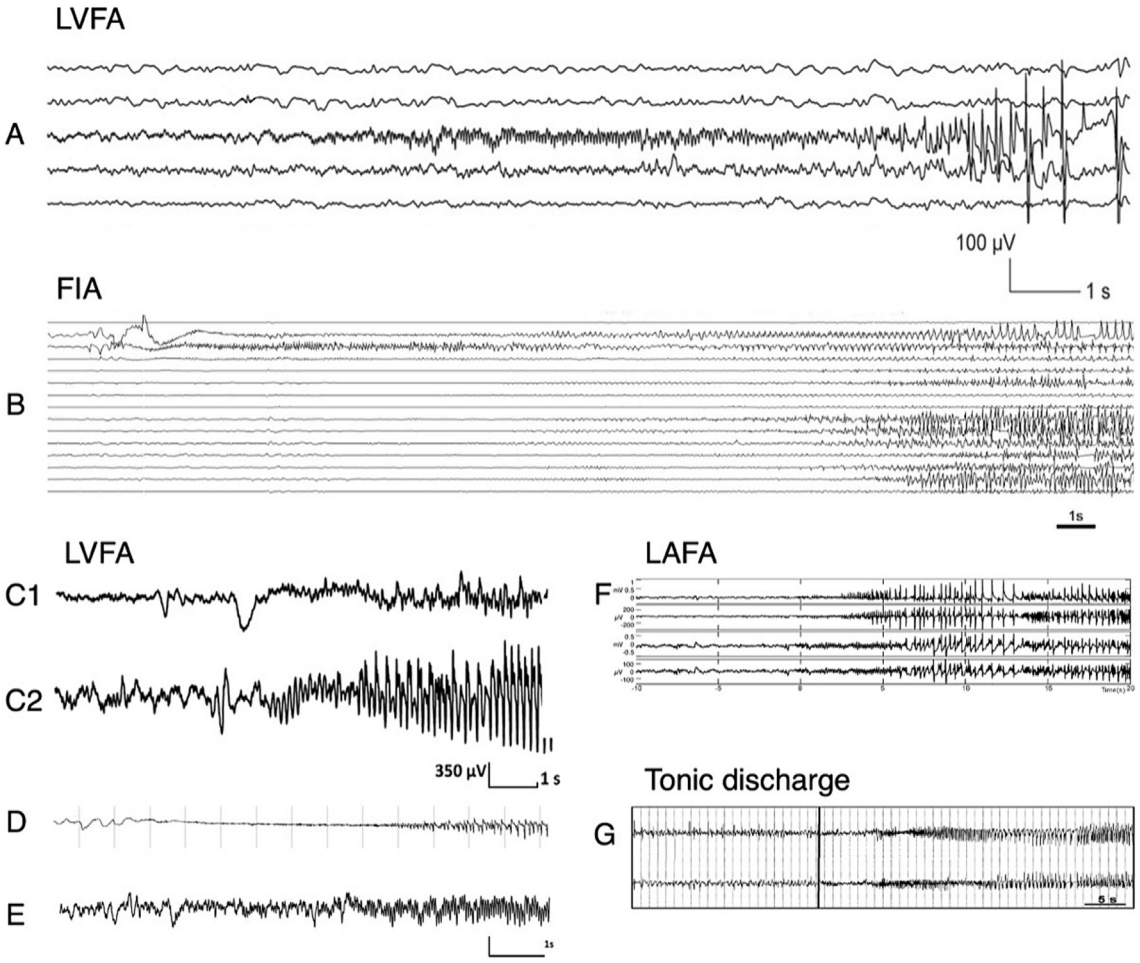


Fig. 3. Depicts divergent terminologies of LVFA across numerous studies: LVFA in A (Perucca et al., 2014), C (Frauscher et al., 2017), D (Fierain et al., 2020), and E (Makaram et al., 2020; FIA in B (Doležalová et al., 2013; LAFA in F (Ilyas et al., 2022); Tonic discharge in G (Bartolomei et al., 2005). LVFA: low-voltage fast activity; FIA: fast ictal activity; LAFA: low-amplitude fast activity.

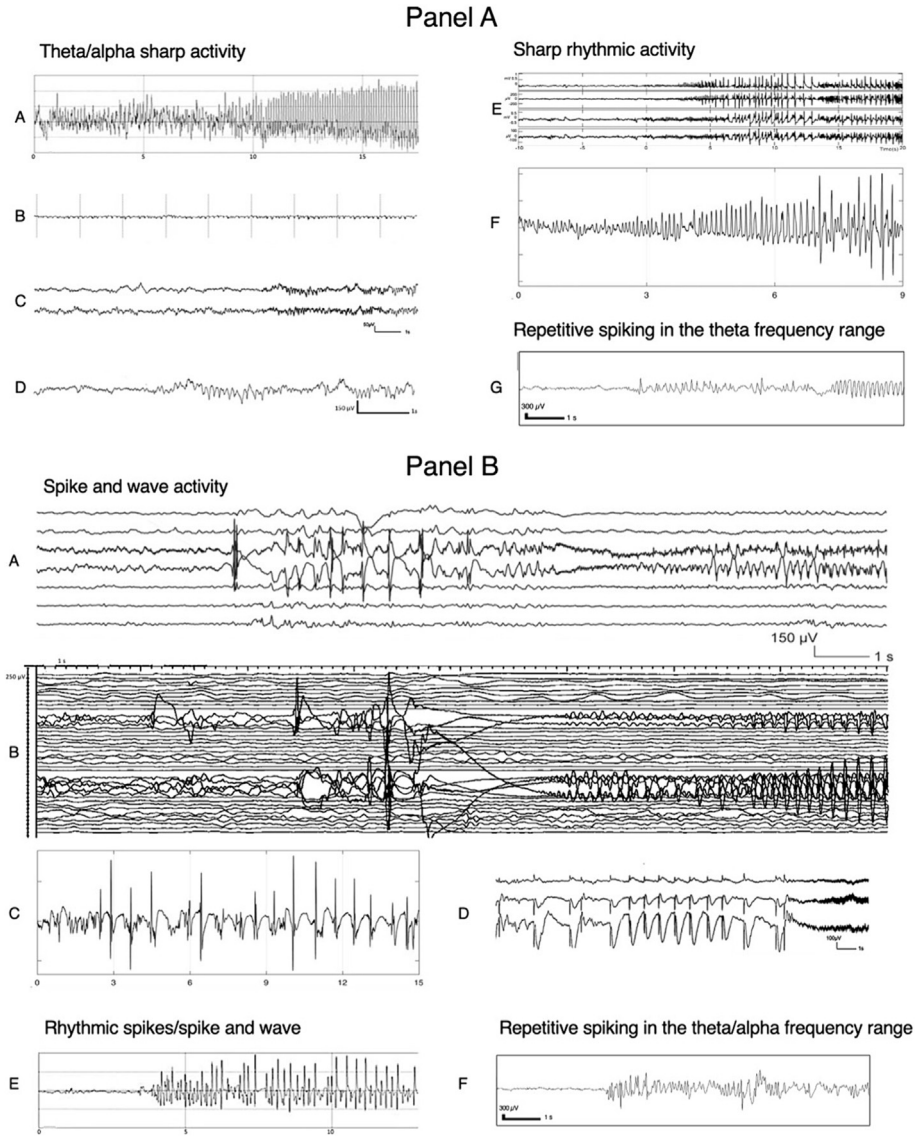


Fig. 4. Depicts divergent terminologies of sharp activity and rhythmic spikes, spike-wave activity across numerous studies. panel A: theta/alpha sharp activity in A (Lagarde et al., 2016), B (Fierain et al., 2020), C (Ferrari-Marinho et al., 2016), and D (Tanaka et al., 2018); Sharp rhythmic activity in E (Ilyas et al., 2022), F (Cui et al., 2022); Repetitive spiking in the theta frequency range in G (Michalak et al., 2023). Panel B: Spike and wave activity in A (Perucca et al., 2014), B (Feng et al., 2020), C (Cui et al., 2022), and D (Ferrari-Marinho et al., 2016); Rhythmic spikes/spike and wave in E (Lagarde et al., 2016); and Repetitive spiking in the theta/alpha frequency range in F (Michalak et al., 2023).

the frequent co-occurrence of LFPS pattern with LVFA (Lagarde et al., 2019a; Schuh et al., 2000; Velasco et al., 2000), in our *meta*-analysis we clustered this pattern alongside other LVFA-associated patterns (Supplementary Material 3). This categorization was established by using definitions and illustrative figures provided in each included study. If the definition in the paper mentioned "Delta-Brush" or "Burst of polyspikes" without specifying the presence of LVFA, we referred to the corresponding illustrative SOP as a reference point for classifying the pattern into the two categories: SOPs with LVFA or SOPs without LVFA (Supplementary Material 3)). SOPs with LVFA, were reported in all included studies, while the other patterns (without LVFA) were reported in 17/22 studies.

Six studies fulfilled our inclusion criteria for evaluating the correlation between SOPs and postoperative outcomes with a minimum follow-up duration of one year. We excluded one study due to its utilization of a LVFA definition cutoff of 8 Hz (Doležalová et al., 2013), significantly lower than the 13 or 14 Hz employed by most papers (Lagarde et al., 2019a, 2016; Perucca et al., 2014) and two others as the reported results were at the seizure and not patient level (Perucca et al., 2014, Cui et al., 2022). All studies provided tables or figures outlining SOP types and the associated surgical outcomes.

Patients in these studies underwent various surgical interventions, including open, resective brain surgery, thermocoagulation, or laser amygdalohippocampectomy. In total, data from 216 patients gathered from three studies (Lagarde et al., 2019a; Liu et al., 2021; Michalak et al., 2023) were included into the *meta*-analysis. The favorable postoperative outcome (proportion of seizure-free patients) was significantly higher in the group of SOPs with LVFA, compared with SOPs without LVFA ($p < 0.001$). The association of seizure-free outcome with the presence of LVFA was weak (effect size estimated using the Phi coefficient = 0.28).

Regarding the correlation between SOP and epilepsy topography, four papers met our criteria (Bartolomei et al., 2005; Di Giacomo et al., 2019; Ilyas et al., 2022; Michalak et al., 2023). In total, from a pooled 178-patient cohort, LFPS was associated more

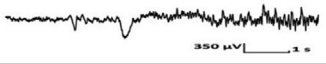
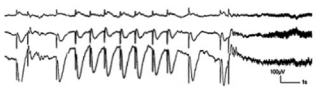
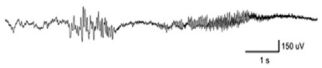
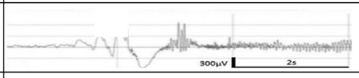
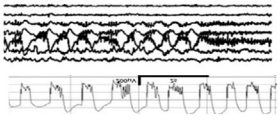
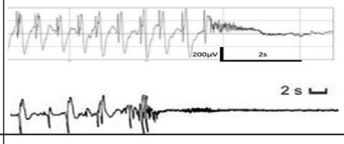
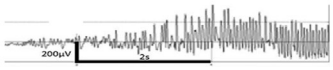
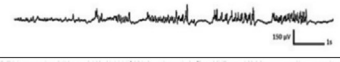
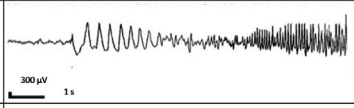
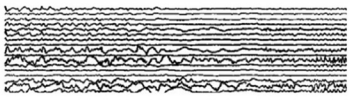
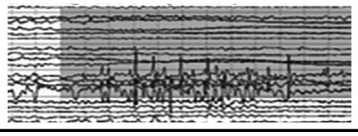
SOPs	Number of studies	Most common reported definition	Other terms	Example
LFPS	20	Low-frequency, high-amplitude spikes having a frequency under 2 Hz, and lasting more than 5 sec.	1. Preictal spiking 2. LFRS* 3. Slow burst 4. Ictal spiking 5. Hypersynchronous activity 6. Slow rhythmic spikes	 Perucca *et al.*2014
LVFA	20	Low voltage (<10 μV) high frequency (>13 Hz) activity.	1. Tonic discharge 2. LAFA 3. FIA	 Frauscher *et al.*, 2017
Sharp activity	16	Sharply contoured rhythmic activity with a frequency ≤13 Hz) typically in the theta/alpha range.	1. Rhythmic sharp activity 2. Theta/alpha sharp waves 4. Slow ictal activity	 Tanaka *et al.*, 2018
Rhythmic spikes/spike-waves	12	Medium- to high-voltage spike-and-wave complexes typically occurring at a frequency of 2–4 Hz (Perucca *et al.*, 2014); Rhythmic spikes or spike-waves, of low frequency (usually >6 Hz and constantly <14 Hz) and with high amplitude (Lagarde *et al.*, 2019a). This pattern may or may not be followed by LVFA.	1. Rhythmic slow spikes 2. Repetitive spikes 3. Repetitive spiking in the theta/alpha frequency range 4. Spike-and-wave activity	 Ferrari-Marinho *et al.*, 2016
Burst of polyspikes prior to LVFA	11	- Burst of polyspikes of high frequency and amplitude and short duration (< 5 seconds) followed by LVFA (Lagarde *et al.*, 2019a). - High frequency and low amplitude rhythmic spikes/polyspikes with short duration (1-3 seconds) prior to LVFA (Di Giacomo *et al.*, 2019).	1. Herald burst 2. Repetitive fast spikes bursts	 Di Giacomo *et al.*, 2019
Baseline shift prior to LVFA	8	Slow wave or baseline shift followed/superimposed by LVFA.	1. Slow wave shift 2. L-type 3. P-type	 Lagarde *et al.*, 2019a
Delta-Brush	6	Rhythmic delta waves at 1–2 Hz, with superimposed brief bursts of 20–30 Hz activity overriding each delta wave (Perucca *et al.*, 2014); Bursts of low-amplitude rapid activity (within gamma frequency bands) (superimposed a low-frequency (delta) activity (Lagarde *et al.*, 2019a). This pattern may or may not be followed by LVFA.	NA	 Perucca *et al.*, 2014 Lagarde *et al.*, 2019a
Preictal activity prior to LVFA	6	- Rhythmic spikes of low frequency (classically ≤3 Hz), high amplitude, and prolonged duration (>5 seconds) followed by LVFA (Lagarde *et al.*, 2019a). - Preictal activity prior to LVFA with high frequency fast discharges (a brief (1-3 s) epoch between rhythmic spikes and LVFA, consisting of high frequency spikes (10 times the preceding rhythmic spikes)) (Chassoux *et al.*, 2000).	Rhythmic spike discharges	 Lagarde *et al.*, 2019a Chassoux *et al.*, 2000
Beta sharp activity	5	Sinusoid activity of beta-band frequency (lower than LVFA (cut-off for LVFA from Lagarde *et al.*, 2019a: 14 Hz)), median initial amplitude (higher than LVFA), and progressive increasing amplitude.	1. Repetitive spiking in the beta frequency range 2. Polyspikes	 Lagarde *et al.*, 2019a
Herald spike or polyspike prior to LVFA	3	A single spike or a polyspike followed by LVFA.	Synchronous spike	 Michalak *et al.*, 2023
Burst suppression	2	Brief bursts of medium- to high-voltage repetitive spikes alternating with brief periods of voltage attenuation.	NA	 Perucca *et al.*, 2014
Delta activity	2	Rhythmic onset of delta activity.	NA	 Michalak *et al.*, 2023
Electrodecrement	2	Increase of frequency, decrease of amplitude (Dolezalova *et al.*, 2013); Attenuation of background amplitude with or without superimposed fast activity (Michalak *et al.*, 2023).	Attenuation of background activity	 Dolezalova *et al.*, 2013
Mixed pattern	1	Repetitive spikes with concurrent attenuation and low voltage fast activity in different regions.	NA	 Steriade *et al.*, 2020

Fig. 5. Depicts the classification, definition, and distribution of the 14 SOPs. SOPs: seizure-onset patterns, LVFA: low-voltage fast activity, LFPS: low-frequency, high amplitude, periodic spikes, LAFA: low amplitude fast activity, FIA: fast ictal activity, LFRS: low-frequency, high amplitude repetitive spikes, LFRS*: low-frequency, high amplitude, rhythmic spikes, NA: not applicable, L-type: low-voltage fast activity superimposed on a slow potential shift, P-type: sharp-onset/sharp-offset transient superimposed on low-voltage fast activity (126 ± 19 Hz).

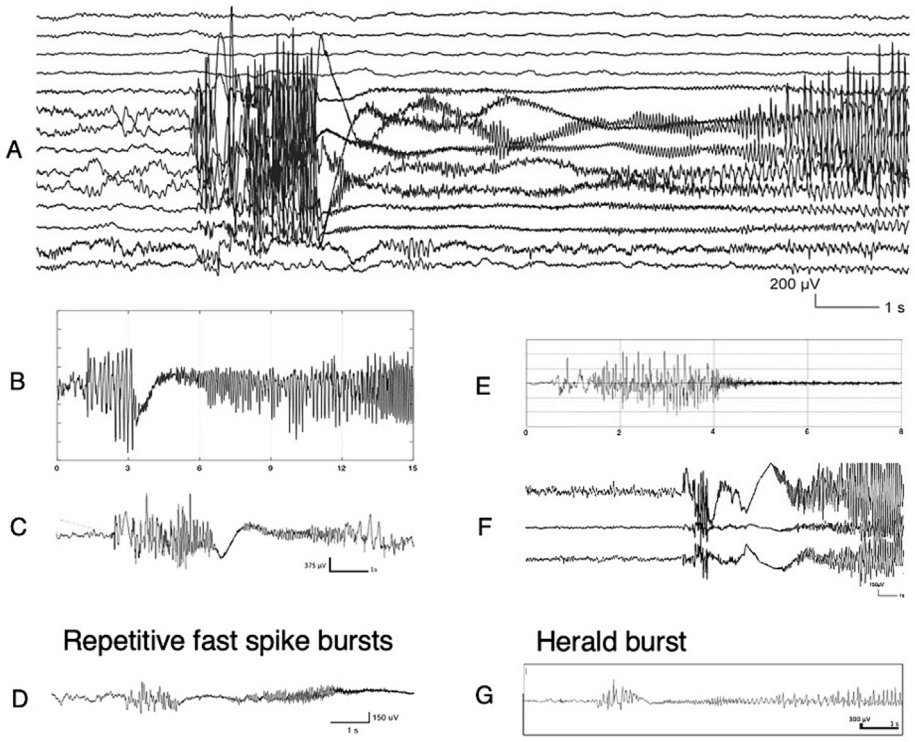


Fig. 6. Depicts divergent terminologies of burst of polyspikes across different studies. Burst of polyspikes in A (Perucca et al., 2014), B (Cui et al., 2022), C (Tanaka et al., 2018), E (Lagarde et al., 2016) and F (Ferrari-Marinho et al., 2016); Repetitive fast spike bursts in D (Di Giacomo et al., 2019); and Herald burst in G (Michalak et al., 2023).

with mTLE than extra-TLE patients ($p < 0.001$, $\chi^2_{gof}(1) = 13.76$), while LVFA was prevalent in neocortical generators (extra TLE) ($p < 0.001$, $\chi^2_{gof}(1) = 21.76$). The "other" SOP patterns, not characterized by LFPS or associated with LVFA, were more frequently in mTLE than extra-TLE ($p < 0.001$, $\chi^2_{gof}(1) = 12.46$). In terms of SOP and etiology, focusing on MCD versus other etiologies, four papers met our criteria (Ferrari-Marinho et al., 2016; Di Giacomo et al., 2019; Lagarde et al., 2019a; Liu et al., 2021). From a pooled 416 patient-cohort, burst of polyspikes was exclusive to MCD ($p < 0.001$, $\chi^2_{gof}(1) = 48$), while other SOPs were less frequent in MCD than other etiologies ($p = 0.02$, $\chi^2_{gof}(1) = 5.88$). No statistical difference was found between the two groups when considering LVFA-SOPs and LFPS patterns. Lastly, considering HS versus other etiologies, five papers met our inclusion criteria (Ferrari-Marinho et al., 2016; Di Giacomo et al., 2019; Lagarde et al., 2019a; Liu et al., 2021; Michalak et al., 2023). From a pooled 474 patient-cohort, LVFA-SOPs as well as other patterns were more frequent in other etiologies than in HS ($p < 0.001$, $\chi^2_{gof}(1) = 236$; $p < 0.001$, $\chi^2_{gof}(1) = 48$). Surprisingly, LFPS was more associated with other etiologies than with HS ($p = 0.002$, $\chi^2_{gof}(1) = 8.97$), suggesting it is non-specific to HS.

4. Discussion

In this review, including 22 studies with more than 1000 patients who underwent SEEG investigations as part of their presurgical evaluation, and providing well-defined SOP descriptions along with corresponding figures, we have highlighted the heterogeneity of SOP terminology. These variations extend beyond the number of SOPs, involving inconsistencies in the terminology of several SOPs, despite referring to the same EEG pattern. Further, we observed that some SEEG terminologies differ from the terminology suggested in the revised glossary of EEG definition (Kane et al., 2017). Finally, our findings confirmed that SOPs with LVFA are indeed associated with a higher likelihood of achieving seizure freedom compared to those without LVFA. However, it is important to note that this association is weak.

4.1. Variability in the number of SOPs and their terminology

Among the 22 studies included in this review, the range in the number of SOPs ranged from 1 to 9. Nevertheless, not all studies investigated different types of epilepsies. Nine studies concentrated on temporal lobe epilepsy (Bartolomei et al., 2005; Cui et al., 2022; Doležalová et al., 2013; Feng et al., 2020; Frauscher et al., 2017; Ilyas et al., 2022; Michalak et al., 2023; Schuh et al., 2000; Velasco et al., 2000), while two studies focused on focal cortical dysplasia (Chassoux et al., 2000; Lagarde et al., 2016), another study on hypothalamic hamartoma (Liu et al., 2021), one on post-traumatic epilepsy (Fierain et al., 2020), and one on post-encephalitis epilepsy (Steriade et al., 2020). Only nine studies embraced a broader spectrum of epilepsy types with all patients having MRI-detected lesions in certain studies (Ferrari-Marinho et al., 2016; Makaram et al., 2020; Perucca et al., 2014; Tanaka et al., 2018) or exhibiting negative MRI results in others (Lagarde et al., 2019b). Nonetheless, the variation in the number of SOPs (ranging from 1 to 9) was also evident in studies centered on mesio-temporal lobe epilepsy (mTLE) (Bartolomei et al., 2005; Feng et al., 2020; Frauscher et al., 2017; Ilyas et al., 2022; Michalak et al., 2023; Schuh et al., 2000; Velasco et al., 2000). Excluding Schuh et al. (Schuh et al., 2000), who exclusively reported one SOP type (LFPS), these studies consistently documented the two most frequently observed SOPs in mTLE: LFPS and LVFA. However, supplementary patterns such as spike and waves, sharp activity, and burst of polyspikes were also mentioned (Feng et al., 2020; Michalak et al., 2023). Discrepancies across these studies may be caused by the emphasis on predominant patterns within the analysis, or the choice to concentrate on specific patterns.

Similarly, among studies that encompassed a broader range of epilepsy types, the number of SOPs ranged from 2 to 8 (Di Giacomo et al., 2019; Gnatkovsky et al., 2019; Lagarde et al., 2019a; Perucca et al., 2014). Gnatkovsky and colleagues identified only two primary SOPs: the P-type originating within neocortical structures across all brain lobes, and the L-type pattern observed almost exclusively in the temporal lobe, both featuring LVFA (Gnatkovsky et al., 2019). In contrast to other studies that not only described LVFA but also additional SOPs like LFPS, preictal spiking, spike and wave, and sharp activity, Gnatkovsky and colleagues considered not just the seizure onset but also its entire duration. Moreover, differences in SEEG indications (particularly in mesio-temporal cases) could potentially contribute to explain the variability in the number of SOPs among these centers.

Regarding terminology, within the 22 studies included, we observed LFPS displaying the highest variability, whereas LVFA retained almost the same designation. In our quest for a standardized SOP terminology for the reported variations of SOPs sharing common definitions, we proposed a unified terminology, resulting in 14 SOPs. This aligns with those previously documented in systematic reviews (Shakhatreh et al., 2022; Singh et al., 2015). A unique aspect of our review is its focus solely on SOPs recorded during SEEG investigation. Distinguishing between SEEG investigations and grids/strips is crucial due to their fundamental differences, primarily in terms of their targets (Chassoux et al., 2012; Roca et al., 2015). This distinction is significant as it could lead to variations in EEG patterns, especially when the generator is deeply located in the brain.

4.2. SEEG SOPs and standard EEG terminology

Among the 14 grouped SOPs, we identified discrepancies between the SEEG SOPs and the standard EEG terminology regarding the bursts of polyspikes followed by LVFA, burst suppression, and delta brush. Terms like paroxysmal polyspikes followed by LVFA for the burst of polyspikes and repetitive spikes/polyspike or bursts of polyspike and wave discharges for the delta brush might be interesting to consider. This observation is important and highlights the necessity for SEEG standardization to facilitate comparison of findings across sites for multicenter study protocols.

4.3. LVFA as a predictor of the surgical outcome

We observed that SOPs with LVFA were frequently present in patients who became seizure-free after operation, whereas a significantly lower proportion of patients became seizure-free when their SOPs were lacking LVFA, such as rhythmic spikes or spike-waves & sharp activity (in the theta/alpha frequency band). These findings are consistent with those reported in multiple studies encompassed by this review (Cui et al., 2022; Doležalová et al., 2013; Lagarde et al., 2019a, 2016; Michalak et al., 2023). However, our findings revealed only a weak association, as indicated by the effect size (Phi coefficient: 0.28). This observation is important considering the prevalent notion that LVFA serves as a strong predictor of surgical outcome (Bartolomei et al., 2008; David et al., 2011; Grinenko et al., 2018; Singh et al., 2015). Through the aggregation of a pooled cohort encompassing over 300 patients, constituting the largest SEEG dataset to date, we highlight the necessity for prudence in regarding LVFA as an unequivocal predictor of surgical outcome. The weakness of this association might explain the inconsistencies in replicating the correlation between LVFA-associated SOPs and surgical outcomes, even within a same epilepsy center's patient cohort (Lagarde et al., 2019a, 2019b, 2016).

Two main confounding factors must be considered when interpreting surgical outcome. The first is related to the extent of the epileptic network, namely, whether it is focal or widespread. The second revolves around the completeness of the presumed EZ resection. These factors were found to predict better surgical outcome than the SOP (Lagarde et al., 2019a, 2016). Indeed, multivariate analyses revealed that only the complete resection of the presumed EZ was able to predict the surgical outcome questioning the association between LVFA-associated SOPs and surgical success (Lagarde et al., 2016). This aligns with the fact that the Marseille's group (Lagarde et al., 2019a, 2016) identified a higher prevalence of LVFA-associated SOPs (79%-83%), while only 55%-47% of patients achieved seizure freedom (Engel I) in their last follow-up evaluation. This discrepancy may be attributed to the preponderance of FCD type II cases, which typically have a more focal epileptogenic network enabling comprehensive resections of the presumed EZ (Chassoux et al., 2012; Tassi et al., 2012). Likewise, patients with a presumed mesio-temporal EZ exhibit higher probability of favorable surgical outcome than those with more diffuse epilepsy networks (Barba et al., 2016; Thom et al., 2010). Consequently, an evaluation of the direct effect of each of these predictors in a larger and boarder cohort of population could yield valuable insights.

4.4. LVFA as a marker of the presumed EZ

Based on our findings and the existing literature, certain SOPs seems to be associated with better surgical outcome even though this association was not strong. Specifically, patterns involving LVFA are more likely to lead to seizure-freedom, signifying them as probably "true" SOPs. In contrast, patterns like theta/alpha rhythmic activity, rhythmic spike, delta rhythmic activity, were predominantly observed in non-seizure-free patients, suggesting their likelihood as "propagation" SOPs. Furthermore, it has been shown that sharp activity is primarily evident in propagation areas (Perucca et al., 2014). However, the existence of LVFA does not necessarily mean "true" seizure onset, and the presence of sharp activity does not invariably signify propagated SOPs. The visualization of both sharp activity and LVFA in propagation areas support this statement (Lagarde et al., 2016; Perucca et al., 2014).

To address the complexity of distinguishing LVFA patterns that belong to "true" SOPs from those associated with propagated patterns, designating a SOP as "true" should encompass not only the requirement of ictal EEG preceding clinical signs but also consider other factors. These factors may include the transition between interictal and ictal activities, as well as the epilepsy topography and the etiology, which has been demonstrated to be closely linked to certain specific SOPs (Di Giacomo et al., 2019; Lagarde et al., 2019a, 2019b, 2016; Perucca et al., 2014; Schuh et al., 2000; Velasco et al., 2000). Precisely, except for specific infrequent SOPs like delta rhythmic and burst-suppression patterns, which require careful consideration and classification as non-SOP patterns, our findings confirmed results from a previous *meta*-analysis (Singh et al., 2015), which identified LFPS as predominantly associated with mTLE, while LVFA is primarily observed in neocortical generators (extra TLE). The burst of polyspikes prior to LVFA, exclusively observed in MCD cases in our *meta*-analysis and in a prior study (Lagarde et al., 2019a), was primarily associated with FCD type II (Di Giacomo et al., 2019; Lagarde et al., 2019a, 2016; Chassoux et al., 2000). In particular, the interictal-ictal continuum pattern characterized by a preictal spiking followed by a brief low and high frequency polyspikes activity prior to the LVFA appears to be more specific to FCD type II ((Chassoux et al., 2000; Di Giacomo et al., 2019). Similarly, Perucca *et al.,* observed the delta brush prior to LVFA only in patients with FCD type II (Perucca et al., 2014). In contrast to earlier findings (Schuh et al., 2000, Velasco et al., 2000), LFPS, in this review, did not show prevalence in HS compared to other etiologies. These results align with Michalak and colleagues (Michalak et al., 2023) and the results from the Milano group (Di Giacomo et al., 2019), both of whom observed no significant asso-

ciation between LFPS and HS compared to non-HS patients. The integration of computational approaches could also offer valuable assistance alongside visual analysis. Specifically, incorporating certain features that might not be readily discernible through visual inspection, such as the modulation of LVFA (down-chirp), which has been shown to be a reliable marker of the presumed EZ, particularly when preceded by a preictal spiking activity (Gnatkovsky et al., 2019; Grinenko et al., 2018), could aid clinicians in their diagnostic practice. However, it is important to note that the presence of preictal activity preceding LVFA, sometimes accompanied by a buildup of activity during the interictal-ictal transition, is more commonly observed in cases of malformation of cortical development (Lagarde et al., 2019a). In other words, when the etiology is suspected to be FCD type II, the absence of preictal activity should warrant attention. On the other hand, in cases where FCD type I is suspected as the underlying cause, diverse patterns like baseline shifts, LVFA, or theta/alpha rhythmic activity patterns may be observed; in case of this pathology, theta/alpha rhythmic activity was correlated surprisingly with favorable surgical outcome in some patients (Di Giacomo et al., 2019). Similarly, no preictal activity pattern was observed in patients with a cavernoma or a post-vascular epilepsy as etiology, and only 1/24 patients had a preictal activity in neurodevelopmental tumors (Lagarde et al., 2019a).

Lastly, despite being more prevalent in malformations of cortical development, the presence of LVFA extends across various etiologies (Di Giacomo et al., 2019; Lagarde et al., 2019a; Perucca et al., 2014). Therefore, it is essential to emphasize that no single pattern can reliably distinguish between "true" seizure onset and propagated patterns. Consequently, presumed "non-seizure-free outcome" SOPs, such as sharp activity, should not be surgically contraindicated solely based on suspicions of propagation patterns.

4.5. Limitations

In addition to the lack of standard SEEG terminology, certain important aspects about SOPs remain underexplored. Notably, the question of the predictive value of mixed patterns within the same seizure and the same patient has not been extensively studied. Many studies focused on analyzing only the predominant pattern (Frauscher et al., 2017; Lagarde et al., 2019a, 2019b, 2016; Makaram et al., 2020; Perucca et al., 2014), and for those who addressed this question, though small cohorts, it has been reported that patients with multiple SOPs had similar outcomes than those with one single SOP (Feng et al., 2020; Michalak et al., 2023).

Another consideration pertains to the baseline shift pattern. Only a few studies analyzed this SOP without applying a band-pass filter (Di Giacomo et al., 2019; Gnatkovsky et al., 2019). It would be beneficial for future studies to specify the minimum band-pass filter required for accurate assessment of this pattern (i.e., hardware high-pass filter at 0.016 Hz).

Confronted with the complexities arising from variations in terminology despite denoting the same EEG patterns, as well as the use of SEEG terminology that were inconsistent with the terminology and definitions in the revised glossary of EEG, the establishment of an international consensus among experts represents an important next step.

5. Conclusion

Our systematic review highlights the need for standardized terminology in the classification of SOPs. Various terms are used to describe similar EEG patterns, and certain SEEG terminologies do not align with the standard EEG terminology. To address these complexities, a broad international collaboration of experts in this field could lead to consensus-based standardized terminology in SEEG, thereby enhancing the quality and relevance of research findings in clinical scenarios, and making large-scale collaborative research possible.

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Conflict of interest

No.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2024.04.016.

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