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SPECIAL REPORT

Basic and preclinical epilepsy research Scientists' perception of clinical epileptology

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Abstract

The interaction between basic science epilepsy researchers and clinical epileptologists is a longstanding issue. Efforts to provide opportunities for a dialogue between preclinical and clinical epilepsy professionals are crucial to reduce the knowledge gap between them and improve the translational success of neurobiology-based research. The International League Against Epilepsy (ILAE) Research and Innovation Task Force circulated a survey to investigate the need for an update on new clinical epilepsy concepts within the basic science community. The 336 respondents included basic scientists (BS), preclinical scientists (PCSs), and/or clinical scientists (CSs). The majority of the 237 BSs/PCSs were engaged in preclinical studies in translational epilepsy research and declared translational research as a priority research interest. Fewer respondents from low-middle-income countries than from upper-middle or high-income countries (40.7% vs 65%) considered translational research a critical aspect of their research. A broad understanding of both clinical and neurobiological aspects of epilepsy was declared by 48% of BSs/PCSs; 96% of CSs declared a superficial knowledge of neurobiology of epilepsy. Most BSs/PCSs were aware that epilepsy is a complex condition that should be investigated with the help of clinical epileptologists, even though concerns were expressed on the relationship with clinicians. A focused training program on emerging clinical epileptological aspects tailored for BSs/PCSs was recommended by 81% of the participants; the majority of respondents preferred either 1- or 2-week in-presence tutoring or continuous online training coordinated by ILAE at the regional/national level. The survey

For affiliations refer to page 72.

also underscored the value of educational programs on neurobiology of epilepsy targeting CSs and low-middle-income countries (LMIC) investigators.

KEYWORDS
basic science, education, epilepsy, preclinical, training

1 | INTRODUCTION

The relationship between basic and clinical science has a long and occasionally controversial history in biomedical research and is a subject of ongoing debate in the epilepsy community. In the early days, the pioneers of experimental epilepsy research were medical doctors by training. This situation changed in the last decades of the last century, when new research tools, new scientific knowledge, and more complex technologies, in tandem with the rapidly accelerating knowledge in clinical medicine, made it difficult to keep pace with the broad available data/literature on various topics and to retain an in-depth understanding of the respective details. Moreover, a progressive separation of working environments and competencies betweenneuroscientists interested in epilepsy and clinical epileptologists has occurred over the last few decades, asemerged during discussion at the International League Against EpilepsyNeurobiologyCommission, at the American Epilepsy Society Research and Training council, at the ILAE/AES Joint TranslationalTask Force, and at international educational events, such as the Courses of the San Servolo Epilepsy SummerSchool1 and the Latin America Summer School on Epilepsy (LASSE;[1] and the Latin America Summer School on Epilepsy (LASSE; https://lasse.med.br/about/). With sporadic exceptions, this divergence was accelerated by the separation of academic careers between clinicians and neuroscientists. The urgent need to reinforce the bridging between clinical and basic sciences strongly reemerged in the current century, to make up for the knowledge gap backlog and to improve the translational success of neurobiology-based research.[2] The issue has been addressed at various national, regional, and international congresses and at epilepsy societies. We could not identify a prior formal survey addressing these issues. Given the abovementioned limitations, reconciling this divergence is not an easy task. The aim of this study is to present an objective picture of the perceived status of clinical epilepsy understanding and of the relationship with clinical epileptologists from the point of view of basic scientists.

The Research and Innovation Task Force (R&I*TF*) of the ILAE proposed an initiative to identify potential strategies and means to improve the translational proficiency of preclinical studies through education and training that aims to bridge the separation between pure preclinical and clinical scientists. Within this framework, the idea was developed to start a training program dedicated explicitly to preclinical basic science experts involved in research activities on epilepsy. The target audience included neurobiologists, neuroscientists, bioengineers, and other professionals who did not have access to clinical epilepsy education during their academic training. The basic concept was to analyze how to provide updated knowledge on general clinical epilepsy and to improve the ability to address meaningful research questions that would facilitate the translation of basic science research into outcomes beneficial for people with epilepsy.

The main objective of this educational project developed by the study group formed within the R&I*TF* (which includes many of the authors of this report and has representatives from all continents) was to create a structured training program potentially accessible across all regions worldwide, in line with one of the fundamental principles of the ILAE mission. The project was structured in five phases: (1) verify the need for a training program on general clinical epilepsy concepts for basic/preclinical scientists with different job positions, geographic locations, and career stages; (2) identify a set of educational objectives critical for this specific training; (3) discuss and design the general scheme/organization for a tailored training program; (4) run pilot training activities, ideally in different regions of the world; and (5) verify, harmonize, and implement the training program. Key performance indicators will be identified to validate the training program post hoc.

To achieve the first aim—that is, assess the need for a clinical training program in epilepsy customized for basic/preclinical scientists—the R&I*TF* study group generated a questionnaire that addressed three main objectives: (1) identify the target audience landscape, (2) collect opinions on translational research in epilepsy and on the interaction of basic/preclinical researchers with the clinical epilepsy environment, and (3) gather views on the ideal structure for the creation of a tailor-made clinical epilepsy training program. As a starting point for the development of the questionnaire, we hypothesized that the following issues are central to a training program in clinical epilepsy: (i) to

Key points

- An online survey was utilized to gather the opinion of basic scientist (BS)/preclinical scientist (PCS) epilepsy researchers worldwide on knowledge and exposure to clinical epileptology.
- Most respondents across all categories, including young students, were engaged in preclinical studies, and declared translation a critical research aspect.
- A broad understanding of both the clinical and neurobiological aspects of epilepsy was reported by 48% of BS/PCS respondents; PCSs, senior, university scientists, and scientists from private companies had higher competency (62%–66.7%).
- Most BS/PCS respondents were aware that epilepsy is a complex condition due to different etiologies that deserves to be better understood with the support of clinical epileptologists.
- Eighty-seven percent of respondents declared an interest in clinical issues and expressed concerns about the relationship with clinical scientists (CSs); there was partial consensus in considering clinicians as scientists (63.1%), even though more than 50% of respondents regularly or often interacted with epileptologists and only 10% never worked with clinicians.
- A training activity on clinical aspects dedicated and customized for BSs/PCSs was considered recommendable by 81% of the participants across all respondent categories.
- The preferred format of this training program was either 1- or 2-week in-presence tutoring (51.1%) or continuous online training (43%), organized by International League Against Epilepsy (ILAE) with regional/national level coordination.
- Gaps in understanding of neurobiological aspects of epilepsy and preclinical research were more pronounced among CSs and investigators from low- and middle-income countries (LMICs).

familiarize with the clinical terminology and update general concepts in clinical epilepsy, (ii) to endorse the awareness on epilepsy as a complex disease, (iii) to emphasize the scientific value of clinical epileptology, and (iv) to advise on the risk of oversimplification of epilepsy-related concepts.

2 | MATERIALS AND METHODS

The questionnaire was designed with the contribution of all R&I*TF* members using *Survey Monkey* (Surveymonkey.com) as an operational tool. The survey text is detailed in the Data S1. The first set of question (*Q1–Q7*) was designed to collect information about the demographics of the targeted audience. The second and third sets of questions (*Q8–Q12 and Q13–Q20*) explored the type of basic research performed by the respondents and their connection with clinical epileptology, respectively. The last group of questions (*Q21–Q24*) directly addressed the interest of basic/preclinical scientists (BSs/PCSs) in an educational activity in clinical epileptology and how it should be organized. Participants were allowed to select multiple responses *to Questions 4, 6, 7, 13, 17, 23, and 24. Questions 8–24* were designed mainly as 5-point Likert scales, although questions 8 and 10 were presented as a continuous 0–100 scoring output (0–20: strongly disagree, 21–40: disagree, 41–60: neutral, 61–80: agree, 81–100: strongly agree). Unless specifically mentioned in the text, the pairs of positive (*agree* and *strongly agree*) and negative (*disagree* and *strongly disagree*) responses were pooled to calculate the percentage values reported in the results detailed below. Each response to *Q8–Q24* was analyzed individually by comparing individual subsets of categories against the mean of all respondents.

The survey was launched on June 1, 2023, and was open for 4 months until September 30. It was accessible on the ILAE website and was disseminated worldwide to potential target audience registers and discussion groups, and via specialized mailing lists at the national, regional, and international levels. The target survey candidate fitted the general definitions of *basic scientist* (BS) or *preclinical scientist* (PCS) with research experience on pathomechanisms of epilepsies at different career stages—from MD/PhD students to senior researchers. In this survey, we considered BS a researcher who aims to generate new theories, tools, or mechanisms to understand better or predict certain epilepsy-related biological processes. In contrast, a PCS performs research in animals or models to test and develop interventions and tools in preparation for future applications in clinical research. *Clinical scientists* (CSs) were considered those involved in research with human subjects.

To analyze the data, we utilized the Survey Monkey data analysis output. Categorical variables were presented using counts and percentages (according to specific sub-groups—see below), and quantitative variables as mean ± standard deviation (SD). Graphs were generated using SPSS Statistics, Microsoft Excel (version 16.82), or JMP Pro 17 (JMP Statistical Discovery LLC, Cary, NC). Data were grouped by category pairs e.g., by gender, basic vs preclinical scientist,

low-middle- vs high-income country according to the World Health Organization classification (https://apps.who.int/gho/data/view.main.LIFEWBLMI?lang=en), or multiple group classes (age range, continent, working position, working environment). Data were expressed as a percentage of the population that answered the specific question or sub-item. Next, we analyzed the answers to the individual questions according to the different subgroups to which the participants belonged (gender, type of scientist, professional role, professional environment, income level of the country of origin). When we observed a percentage variation larger than ±10% from the general cohort, we performed a two-tailed Pearson chi-square test (χ^2). When the participant belonged to more than one subgroup, we performed a multivariate ordinal logistic regression analysis. Data from fewer than five respondents were plotted differently in graphs (checkered patterns in Figures 3–6). A $p < .05$ was considered statistically significant. Statistical analysis was performed using SPSS Statistics (IBM Corp. Released 2017. IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp.) or JMP Pro 17.

3 | RESULTS

Responses to *Q1–Q7* formed the core data that identified the demographics of the survey respondents, in terms of age, working position, gender, professional environment, and geographical origin. The overall output of the survey for all participants is illustrated in Data S2. The survey was completed by 336 respondents. Of these, 237 met the inclusion criteria for the target audience (identified as BS or PCS—with the exclusion of pure CS). A specific section in the Results compares the most relevant differences in the responses among the BS/PCS and CS groups.

3.1 | Survey responses from respondents identified as BS/PCS

BS/PSC respondents (53.6% male; Figure 1C) displayed a heterogeneous age range (Figure 1A). Among the participants, 185 identified as BSs (78.1%) and 122 as PCSs (51.5%; Figure 1D); 28 PCSs (11.8%) also defined themselves as CSs. One hundred seven respondents identified exclusively as BS (45.1%of the sample), whereas respondents identified as BS/PCS, BS/CS, or CS/PCS were sorted as PCS (see Figures 3–6). As shown in Figure 1E, most respondents worked in research institutes (159; 67.1%), 106 (44.7%) in universities, 11 (4.7%) in non-academic hospitals, and 15 (6.3%) at private companies. Respondents held various positions in their working environment, as summarized in Figure 1B: 42 PhD and PhD/MD students (17.7%), 44 postdoctoral fellows (PD, 18.6%), 40

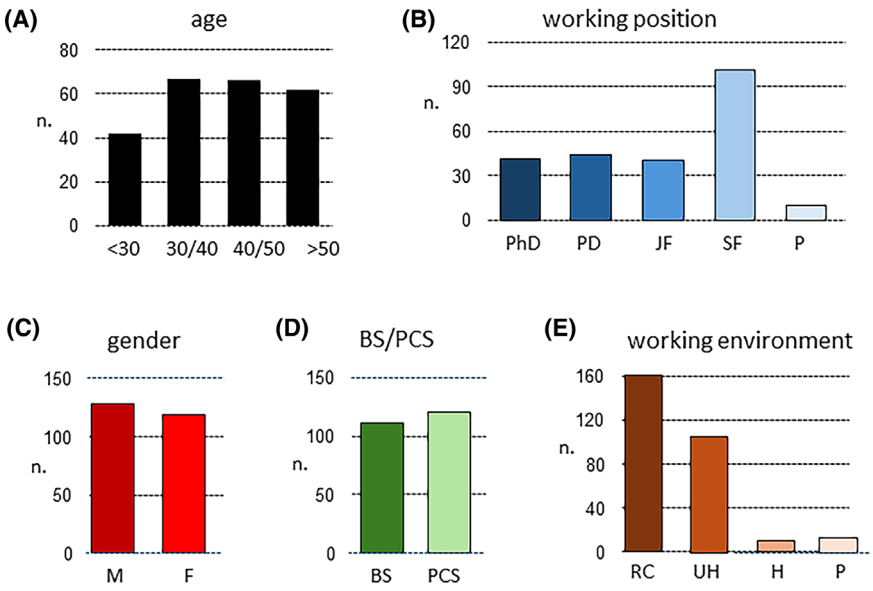

FIGURE 1 Demographics of the scientists who participated in the survey. All data are expressed as number of respondents for each category. (A) Age distribution: Younger than 30 years old, between 30 and 40, between 41 and 50 and above 50 years old. (B) Distribution of working positions expressed by different intensities of blue shading, from students (both PhD and PhD-MD students), postdoctoral fellows (PD), junior scientists/faculties (JF), senior scientists/faculties (SF) and employees of private companies (P). (C) Male (magenta) and female (bright red) distribution. (D) Number of respondents self-identified as basic scientists (BS; light green) or preclinical scientists (PCS; dark green). (E) The working environment of respondents is marked by different intensities of brown: Research centers (RC), university hospitals (UH), non-university hospitals (H), and private companies (P). The column color codes are maintained in the following Figures 3–7.

independent junior scientists/faculty (JF, 16.9%), 101 senior scientists/faculty (SF, 42.6%), and 10 research scientists employed in the private environment (P, 4.2%). The salaries for the above positions were supported by different sources that included research grants (119, 50.2%), institutional funding (101, 42.6%; of these 49 from national governmental funding), and clinical revenue (13, 5.5%).

The participation from different continents was uneven, with most respondents from Europe (45%), followed by North America (22%), Latin America (14%), Asia (9%), Oceania (8%), and Africa with the Eastern Mediterranean region (2%; Figure 2A; details by countries in Figure 2C). Of the 38 countries represented in the survey, 16 (37.2%) were defined as low-, low-middle, and upper-middle income countries according to the World Health Organization classification (defined as low-middle income countries—LMICs in Figures 2–6) and 27 (62.8%) were recognized as high-income countries (HICs). Fifty-eight (24.5%) and 179 (75.5%) of the survey respondents were from LMICs and HICs, respectively (Figure 2B). A more detailed analysis of all possible demographic variables identified by the responses to *Q1–Q7* is beyond the objectives of this report.

For the analysis of the second part of the questionnaire (*Questions 8–23*), we compared the overall population scores (black columns in Figures 3–6) with the following five categories: gender (red/orange columns in Figures 3–6), working position (blue-shaded columns), country income (gray-shaded columns), qualification as BS or PCS (green-shaded columns), and working environment (brown-shaded columns). Checkered color patterns were used when data from fewer than five respondents were counted for each item (Figures 3–6). The analysis revealed responses that either were homogeneous among the different subgroups or varied according to specific demographic/category features, as mentioned and detailed in the following paragraphs. The age and working position subgroups showed similar response pattern distribution; for this reason, only differences among working positions were further analyzed as an approximation of age classes. Large variability was based on respondent location or income level country. The number of respondents

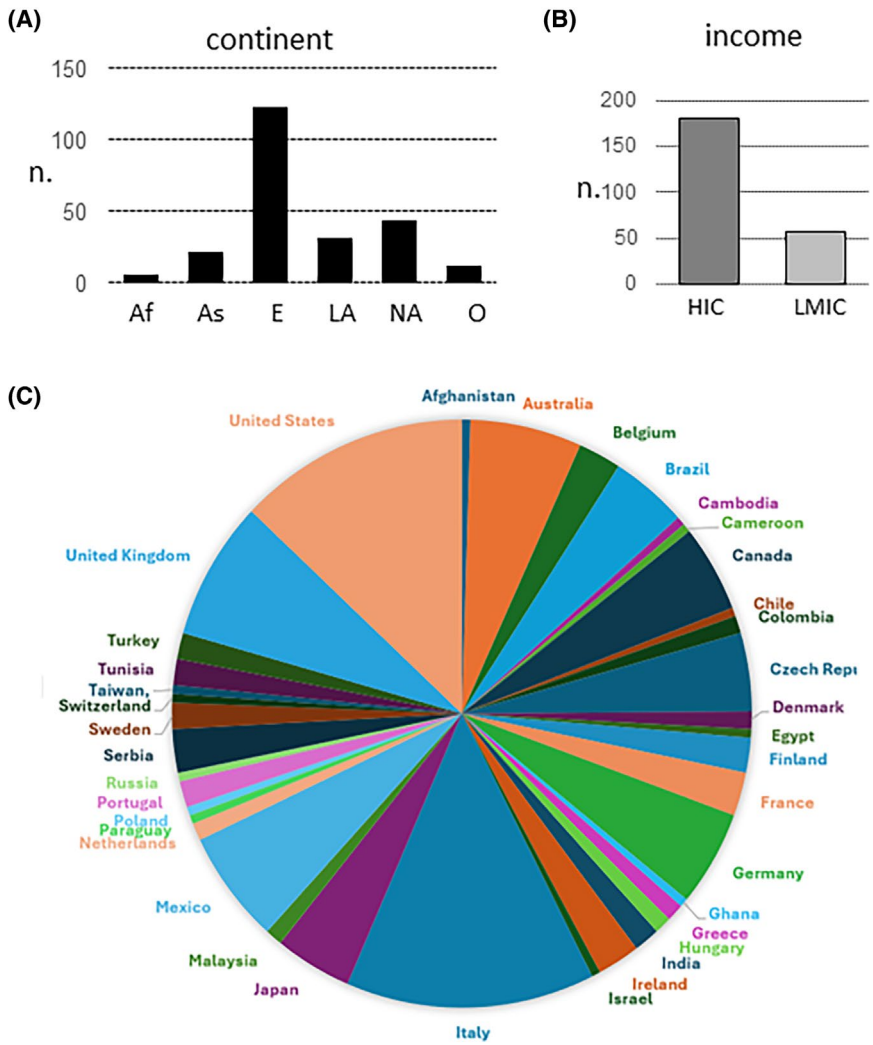

FIGURE 2 Origin of survey participants. (A) Continent of origin: Africa (Af, which includes Eastern Mediterranean Countries), Asia (As), Europe (E), Latin America (LA), North America (NA), and Oceania (O). (B) Number of participants originating from high-income countries (HICs, dark gray) and from low-medium-upper income countries (defined as low-medium income countries—LMICs, light gray) according to the World Health Organization. (C) Distribution of the participants by country of origin. The column color code of B is maintained in the following Figures 3–7.

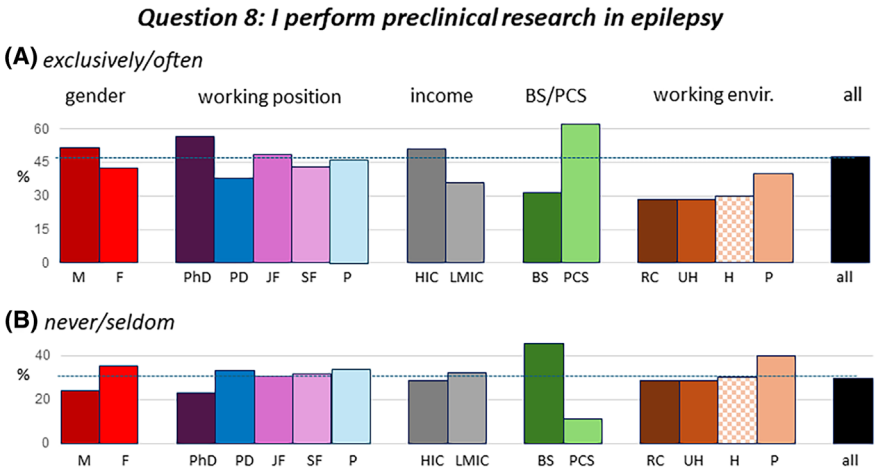

FIGURE 3 Distribution of responses to *Question 8*: *I perform preclinical research in epilepsy*. Percent distribution for each of the five categories of respondents indicated on top (color codes that represent categories are detailed in Figures 1 and 2) who responded either *exclusively/often* (Likert points 4 and 5; A) or *never/seldom* (Likert points 1 and 2; B) to the 5-point Likert scale (see Data S1). Likert scale value 3 is not illustrated. The black column on the right and the dotted horizontal lines represent the average response of the whole population of respondents (all). Checkered color patterns were used when data from fewer than five respondents were counted for each item.

from different continents was also unevenly distributed, so we restricted the analysis to the comparison between LMICs and HICs. The source of support for the BS/PCS remuneration (*Q7*) was not further analyzed. No significant differences were observed between male and female respondents for all survey questions, with the exceptions mentioned below. Of interest, differences were found by comparing respondents who self-defined themselves as BSs vs PCSs. Specific divergences between different subgroups of participants are described in the following paragraphs, focusing mainly on national income differences, working positions, and personal assignment as BSs vs PCSs.

Responding to *Question 8*, the majority of participants across all categories exclusively or almost exclusively performed preclinical studies in translational epilepsy research (Figure 3A; see also Data S2). More PCSs than BSs (62.1% and 31.5%, respectively, $p < .001$) performed almost exclusively preclinical research studies (green columns in Figure 3) vs 47.3% of the whole population. The trend of the response to *Q8* was different in LMICs vs HICs, where 50.9% of HICs vs 35.8% of LMICs, respectively (87 vs 19 respondents) performed exclusively/often preclinical studies (dark and light gray columns in Figure 3A).

Almost all contributors recognized the value of translational research (*Question 11*) to impact on clinical practice (96.9%) and to advance science (93.2%), and most acknowledged that translational studies enhance the chances of receiving funding and publishing in high-impact journals (76.4%; but 46% for researchers who worked in private companies). In response to *Questions 9 and 10* (see Data S2), all categories declared translational research as a priority research interest (67% on average; 80.4% of PCSs vs 52.8% of BSs; lower than average—50%—for MD/PhD students). The interest in epilepsy research was supported by ongoing research grants focused on epilepsy for 70.5% of senior scientists (vs 38.1%, 37.7%, and 46% of MD/PhD students, postdocs, and BSs working for private companies, respectively). On average, 76% declared that translational research facilitates the chance to obtain a research grant—female respondents were more positive than male respondents in this regard (83.8% vs 69%). This element was relevant for only 46% of BSs working in private companies. A similar distribution of responses to *Q9/10* was observed in both LMICs and HICs. Most respondents across categories were engaged in translational research (*Question 12*; see Data S2) because they had translational grant funding (53%; unsurprisingly, this value was 30.6% for MD/PhD students), enjoyed the interaction with clinicians (81.7%), and valued the possibility of a positive impact on patient care as a result of their research activities (67%). These aspects were also appreciated by BSs working in private companies (80%) and by younger scientists. Both senior and junior established scientists confirmed a direct involvement in translational research activities grounded in ongoing and established research projects (58%).

In response to *Question 13* (Figure 4; see also Data S2), on average, 48% of the participants declared a good understanding of both neurobiological and clinical aspects of epilepsy (Figure 4A), with a higher prevalence for senior faculty/scientists (64.4%) and PCSs (62.3%) working in both university centers (64.2%) and private companies (66.7%). Postdoctoral fellows declared a lower percentage

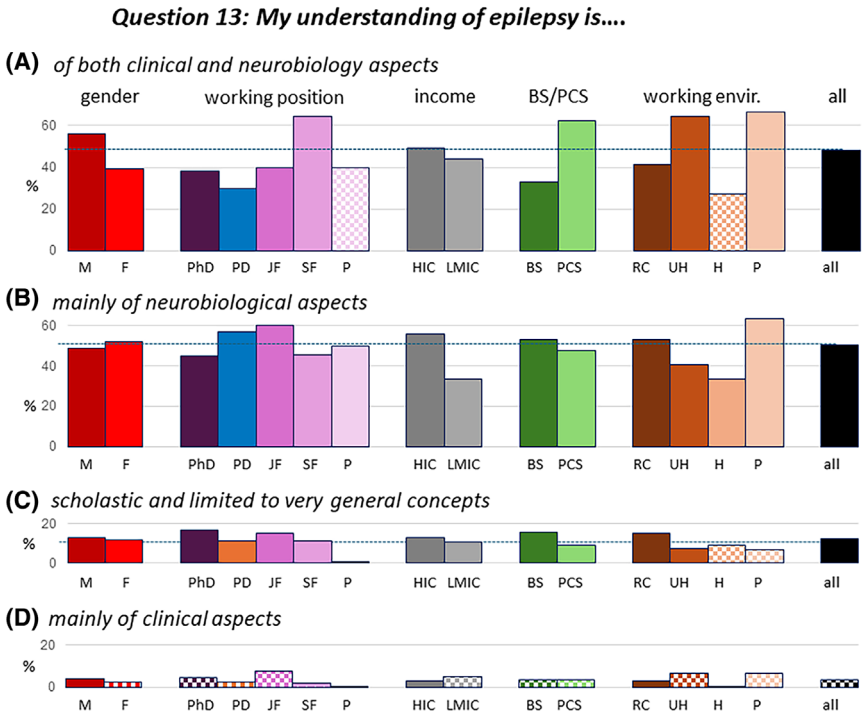

FIGURE 4 Distribution of responses to *Question 13: My understanding of epilepsy is....* Percent distribution for each of the five categories of respondents indicated on top (color codes that represent categories are detailed in Figures 1 and 2) who indicated that they agree/strongly agree (Likert points 4 and 5) with the following items: *Both on clinical and neurobiology aspects* (A), *mainly of neurobiological aspects* (B), *scholastic and limited to very general concepts* (C), or *primarily on clinical epilepsy* (D). The black column on the right and the dotted horizontal lines represent the average response of the whole population of respondents (all). Checkered color patterns were used when data from fewer than five respondents were counted for each item.

of mixed neurobiology/clinical competence. Fewer respondents from both university and non-university hospitals declared an exclusive competence in the neurobiology of epilepsy (40.6% and 33.3%, respectively, compared to 50.2% in the whole population; Figure 4B), which was higher for scientists working in private companies (63.2%; rightmost column in the working environment category of Figure 4B). Of all LMIC respondents, 33% declared an exclusive knowledge of neurobiological aspects of epilepsy, a value lower than the average 50.2% of all the categories. Overall, only 12.2% had scholastic knowledge of epilepsy, with an even distribution among different categories (Figure 4C). As expected from our selected call addressed to BSs and PCSs, only eight respondents declared a primarily clinical understanding of epilepsy (Figure 4D).

Answering *Question 14*, virtually all participants were aware that epilepsy is a complex condition due to different etiologies, which deserves to be better understood with the support of clinical epileptologists (Data S2). Most respondents (56.5%; but 31.3% in LMICs and 45.2% among MD/PhD students) declared that epilepsy is not simply a straightforward condition characterized by altered excitability, whereas more LMICs than HICs agreed with this statement (57% and 20.9%, respectively, $p < .001$).

With regard to the relationship with clinical epileptologists (*Question 15*; Data S2), the participants were largely neutral when asked if clinicians have a good understanding of or are interested in preclinical research. There was partial consensus in considering clinical epileptologists as scientists (63.1%), and that clinicians have an evident patient-based knowledge that is unavailable to BSs (79.4%). These opinions were based on regular or frequent interactions with clinical epileptologists among all subgroups and in all global regions (response to *Question 16*). Only about 10% of interviewed BSs and PCSs either never worked or did not work anymore with clinicians on epilepsy-related projects (Data S2). MD/PhD students and LMIC respondents interacted less with clinicians (~25%) than the whole population (39.2%). Both industry researchers and senior scientists stated that they regularly interact with clinical epileptologists (50% vs 39.2% in the whole population).

BSs and PCSs collaborate with clinicians (*Question 17*; Figure 5 and Data S2) to develop research on clinically relevant topics (57.8% on average; Figure 5A); this was more relevant for 71.1% of senior researchers and 73.3% of BSs working in private companies **than** for MD/PhD students and postdocs (40.5% and 47.7%, respectively)

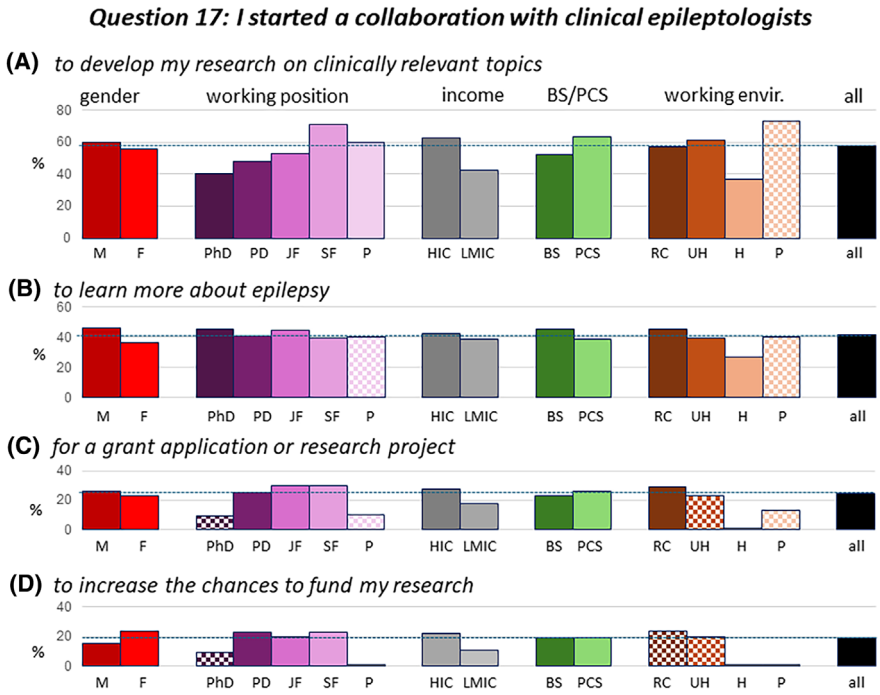

FIGURE 5 Distribution of responses to *Question 17*: I started a collaboration with clinical epileptologists. Percent distribution for each of the five categories of respondents indicated on top (color codes that represent categories are detailed in Figures 1 and 2) who indicated that they agree/strongly agree (Likert points 4 and 5, see Data S1) with the following subitems: *To develop my research on clinically relevant topics* (A), *to learn about epilepsy* (B), *for the need of a grant application or research project* (C), *to increase the chances of funding, since grants ask for clinical translation* (D). The black column on the right and the dotted horizontal lines represent the average response of the whole population of respondents (all). Checkered color patterns were used when data from fewer than five respondents were counted for each item.

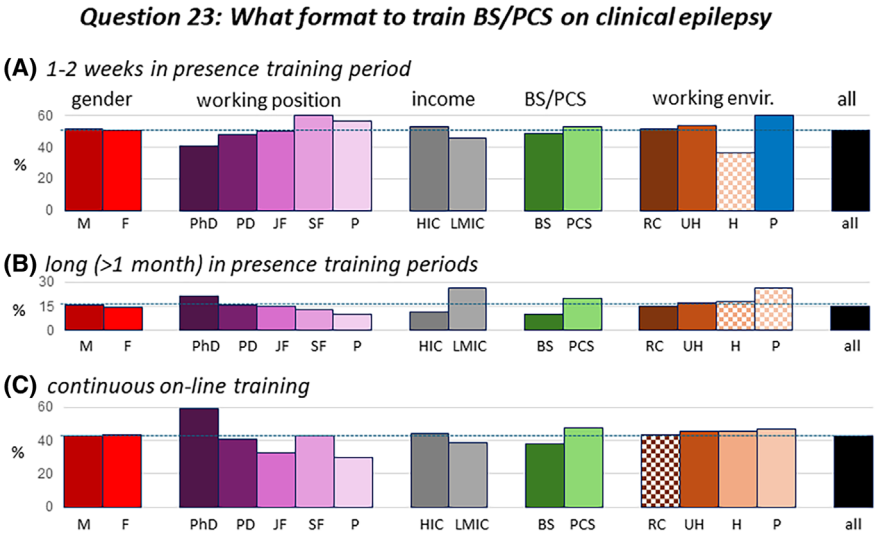

FIGURE 6 Distribution of responses to *Question 23: What format should be utilized for a training program on clinical epilepsy tailored to BS/PCS researchers?* Percent distribution for each of the five categories of respondents indicated on top (color codes that represent categories are detailed in Figures 1 and 2) who indicated (A) *1–2 weeks in presence training period*, (B) *long (>1 month) in-presence training periods*, (C) *continuous on-line training*. The dotted horizontal line represents the averageresponse of the whole population. Checkered color patterns were used when data from less than five respondents were counted for each item.

and LMIC respondents (42.1% vs 62.8% in HICs). Other motivations to collaborate with clinicians were the current need to develop already funded joint projects (24.5%; even less attractive for scientists working in private environment and non-university hospitals; Figure 5C) and the opportunity to increase funding success by performing

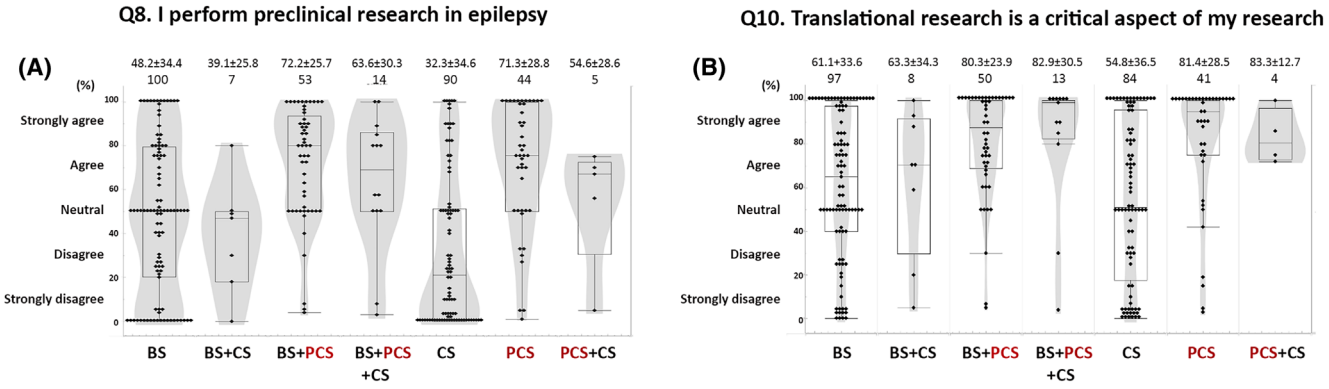

FIGURE 7 Self-identification as BS, PCS, or CS influences, but does not define, the degree of performing preclinical or translational research. (A) Responses to Q8 ("*I perform preclinical research in epilepsy*") according to the type of BS/PCS/CS expertise, grouped by BS/PCS/CS self-identification in Q4, are presented as violin plots. Preclinical research is performed across all groups, but with higher odds ratios for responding agree/strongly agree in the PCS groups (odds ratio 3.81, $p < .001$) and lower odds ratios in the CS groups (odds ratio .438, $p = .013$). (B) Responses to Q10 ("*Translational research is a critical aspect of my research*") according to the type of BS/PCS/CS expertise, as declared by the Q4 responses, are presented as violin plots. Self-identification as PCS, with or without additional expertise in BS or CS, increases the degree to which investigators consider translational research a critical component of their research (Q10). The numbers over each violin plot show means ± standard deviation and number of respondents per group.

clinical translation work (19.0%; Figure 5D). Among those who answered *Question 18* (Data S2), 71.6% stated that epilepsy congresses provide useful information for daily work (only 32.3% of BSs working in private companies), whereas 48.3% endorsed affirmed that epilepsy meetings are attractive to BS (26.6% and 25.1% were either neutral or disagreed); postdoctoral fellows were less keen to agree that epilepsy congresses provide helpful knowledge for their daily work (54.3% vs 71.6%), whereas industry researchers the opposite point of view was held (88.9%).

Several factors interfere with the intent or consideration to interact with clinicians in the field of epilepsy (*Question 19*) that are not uniformly perceived across different respondent subgroups, except for gender and country income. Of interest, 87% of respondents declared an interest in clinical issues. As expected, difficulties in understanding clinical language were more relevant for BSs compared to PCSs (65.1% vs 45.2%, respectively, $p = .005$). In addition, the respondent occupation influenced the answers to this question ($p = .009$). In fact, although MD/PhD students and BSs/PCSs working in university centers have fewer issues in understanding clinical language (64% and 68.1%, respectively, vs 55.8% in the average population), postdocs and junior faculty reported language difference issues more often (42.9% and 40%, respectively). Multivariate ordinal logistic regression analysis indicated that the predictor variables BS ($p = .001$), junior faculty/scientist ($p = .004$), and post-doctoral research fellow ($p = .004$) had a significant effect on the specific answer to *Q19* **and** revealed a very similar response **to** the question concerning difficulties in considering clinical details. Only 14% of respondents perceived that methodological approaches between clinical and basic research were not relevant to limit interest in clinical work. Time restriction was an issue for many participants, particularly for MD/PhD students (63.3% vs average 45%). About half (45.2% vs overall 34.5%) of the MD/PhD students perceived clinicians as not interested in basic science research aspects, whereas 47.2% of senior scientists had the opposite opinion (vs 37% on average disagreed that clinicians are not interested in basic science). According to the survey responses to *Question 20* (Data S2) the interactions with clinical epileptologists could be improved, in order of preference, by sharing an understanding of appropriate techniques/methodologies (94%), by promoting multi-modal studies that consider both preclinical and clinical aspects (93.6%), by enhancing interdisciplinary clinical-preclinical training activities (93.1%), by enhancing the attractiveness of epilepsy meetings for basic scientists (90.7%; less relevant for 78.6% of BSs working in private companies), and by planning regular meetings to discuss clinical and preclinical topics (87.2%). The need to improve the terminology barrier (on average 79.8%) was more perceived by LMICs than HICs (92.9% vs 76.42%). The industry researchers were less interested in proposing solutions to improve the interaction with clinical epileptologists.

The last four questions (*Q21–Q24*) explored the interest in a training activity on clinical aspects of epilepsy dedicated to and customized for BSs and PCSs, that was valued as very attractive by 77% and recommendable by 83.1% of the participants (*Question 21*). Of interest, 100% of BSs working in private companies supported such dedicated training. MD/PhD students were less than average (73.8% vs 83.1%) keen to recommend a training activity

dedicated to BSs/PCSs (*Question 22*); 24.6% and 11.1% of respondents in LMIC vs HIC countries declared not to be interested in the proposed training. No significant differences were found for *Questions 21 and 22*. As shown in Figure 6, in their responses to *Question 23* (see also Data S2), participants favored either brief in-presence (1–2 weeks; 51.1%; Figure 6A) or long-term online training (43%, Figure 1C), and less frequently the longer in-presence training option (>1 month; 15.2%; Figure 6B). It is notable that LMIC participants showed a stronger preference than HIC participants for long-term in-presence training ($p < .01$), although this option was still the least favorite of the three, MD/PhD students reported a preference for online training (59.5% vs mean 43%; Figure 6C) and favored fewer in-presence short trainings (40.5% vs average 51.1%); the opposite trend was observed for industry researchers (60% for short in-presence and 30% for online training). *Question 24* inquired about how the training should be organized (Data S2): a similar subgroup of respondents expressed a preference for either regional (36.3%) or national (43.1%) training events coordinated (but not organized) by ILAE, or a training centrally controlled by ILAE (41.5%; university workers were more interested in 49.1%). Only 3% of respondents did not consider ILAE coordination necessary and 79.4% supported the regional/national involvement with ILAE coordination. Postdoctoral scientists responded less often that such training should be organized by ILAE ($p < .02$), and when considering gender, male respondents showed a preference for training organized at a national level ($p < .01$).

In the survey section open to free comments, worries were expressed about potential problems during the interaction with clinicians and the likelihood that it was necessary to dedicate long periods (weeks/months) to clinical training that does not specifically relate to laboratory activities. The organization of ad hoc workshops on training of BSs/PCSs prior to the ILAE conferences was proposed, even though the ILAE environment was perceived as conservative and not ideal for catalyzing interdisciplinary activities. Participation in the clinical staff meetings was considered useful. It was also suggested that the cost of conferences could be reduced for preclinical researchers who do not have funding opportunities like clinicians.

3.2 | Preclinical and translational research is not an exclusive feature of researchers identified as PCSs or BSs

We queried the extent to which self-identification as PCSs reveals whether an investigator performs preclinical (*Q8*) or translational research (*Q10*), including all respondents to our survey ($n = 336$; Figure 7). Although PCSs generally showed a higher agreement rate in performing preclinical research, there was significant spread in the responses across groups (Figure 7A). PCSs (pure or mixed expertise) were more likely to agree/strongly agree with *Q8* (odds ratio [OR] 3.81, $p < .001$). In contrast, self-identification as CSs (pure or mixed) had a negative effect on the degree of performing preclinical research (OR 0.438, $p = .013$), whereas BSs (pure or mixed expertise) had an OR of 0.868 ($p = .646$). Our survey was not designed to explore the underlying reasons for these differences. However, the results underscore the importance of targeting PCSs, BSs, and CSs with initiatives that target preclinical research.

To identify the audience that should be targeted by educational programs pertinent to translational research, we analyzed all 336 respondents to *Q10*. Most (79%) of the respondents considered that translational research was a critical component of their research (neutral, agree, strongly agree), regardless of whether they perceived themselves as BSs, PCSs, or CSs (Figure 7B). However, the self-identification as BSs, PCSs, or CSs significantly affected these responses (Pearson, $p = .004$). PCSs had the highest proportion undertaking translational research (BS + PCS + CS, 84.6%; PCS only, 90.2%; BS + PCS, 94%; PCS + CS, 100%), whereas groups not identified as PCSs had lower rates (CS only, 66.7%; BS + CS, 75%; BS only, 77.3%). The likelihood of considering translational research as critical was greater in BSs of mixed expertise (also self-identifying as PCSs or CSs; Fisher's exact test, $p = .038$) than in pure BSs. The degree to which respondents considered translational research a critical component was greater among PCSs (with or without BS or CS background, range 80.3%–83.3%) than among BSs and/or CSs (54.8%–61.1%; Kruskal–Wallis, $p < .0001$). These suggest that educational programs targeted at improving translational research should have a wide reach, capturing researchers of diverse backgrounds (BSs, PCSs, CSs).

3.3 | Clinical scientist perspective

In most questions, the CS responses followed the same trends as those of the non-CS groups, with the following exceptions. Fewer CSs were engaged in translational research because they had a research grant (CS 39.6% vs non-CS 52.9%; Fisher's exact test, $p = .032$) or because it was their priority research area (CS 52.7% vs non-CS 65.3%; Fisher's exact test, $p = .039$) or because they would like to see the impact on patient care (CS 73.45% vs non-CS 91.37%; Fisher's exact test, $p < .001$; *Question 12*). Most CSs did not have a good understanding of neurobiological aspects of epilepsy (96%), whereas most non-CSs did (56%; Fisher's exact test,

$p < .001$) but had a better understanding of clinical aspects of epilepsy (33%) than non-CSs (1%; Fisher's exact test ,$p < .001$; *Question 13*). More CSs believed epilepsy is a straightforward condition characterized by enhanced excitability (52%) than non-CSs (26.7%; Fisher's exact test, $p < .001$; *Question 14*). Although a minority of CSs declared a good understanding of preclinical science (38%), this was still better than the rate of non-CSs (19%; Fisher's exact test, $p < .001$; *Question 15*). As expected, fewer CSs declared that clinical epileptologists have better patient-based knowledge than they do (51%) or than non-CS respondents (82%; Fisher's exact test, $p < .0001$; *Question 16*). More CSs collaborated with clinical epileptologists because they were also clinicians (CS 75% vs non-CS 9%, $p < .001$; fewer CSs did so to develop clinically relevant topics (CS 45% vs non-CS 64%, $p < .0001$; *Question 17*). More CSs found the epilepsy congresses helpful in providing information used in their research (CS 87.9% vs non-CS 68.5%, $p = .0003$) and attractive to basic scientists (CS 61% vs non-CS 46.9%, $p = .025$; *Question 18*). Fewer CSs stated that they do not understand the clinical language (CS 9.4% vs non-CS 14.2%, $p = .0033$), that it is difficult to consider clinical details (CS 7.3% vs non-CS 20.3%, $p = .005$), or that clinicians do not understand their research (CS 13.3% vs non-CS 36.3%, $p < .0001$; *Question 19*). Most CSs (68%) favored the proposal of a training program on clinical epilepsy targeting BSs/PCSs, and their responses were split among the continuous online training (34.4%), 1–2 week-long course in-presence training (32.8%), and long (1 month) in-presence training (14.4%; *Question 23*). CS responses were almost evenly split among central ILAE coordination (31.9%) and ILAE coordination at the regional (31.9%) or national (27%) level. Although still the majority of CS respondents rejected the option of no ILAE involvement in coordinating these courses (88%), a higher percentage of CSs (12%) than non-CSs (1.69%) responded that ILAE should not be involved in coordinating these training courses (Fisher's exact test, .026).

3.4 | Perspective from LIC/LMIC/UMIC/HIC investigators

Including all respondents increased the representation from LMICs ($n = 32$) and Upper Middle Income Countries (UMICs) ($n = 70$). A greater representation of CSs was noted among the respondents from UMICs (53%), LMICs (71%), or LICs (67%) than from HICs (27%; nominal logistic fit, $p < .001$), and many were pure CSs (LIC 67%, LMIC 66%, UMIC 41%, vs HIC 19%). There were only three respondents from LICs, and none were performing preclinical research or considered translational research critical for their research; 56% of LMIC and 63% of UMIC respondents performed preclinical research at some level (*Q8* responses neutral – strongly agree), vs 68% of HIC respondents (no significant difference). Translational research was critical for 40.7% of LMIC vs 65.2% of UMIC and 65.5% of HIC respondents (Pearson chi-square, $p = .04$; *Question 10*). LMIC respondents showed a lower level of understanding (29%) than UMIC (53%) or HIC (48%) respondents for both clinical and neurobiological aspects (Pearson $p = .002$). Higher rates of LMIC (56.5%) and UMIC (66.1%) respondents than HIC respondents (23.8%) thought epilepsy is a straightforward condition of enhanced excitability (Pearson, $p < .0001$; *Question 14*). Most LMIC respondents felt that epilepsy congresses are attractive to basic scientists (81.8%) compared to UMIC (58.6%) or HIC respondents (46.5%; Pearson, $p = .0036$). In *Question 21*, the value of a training program on clinical epilepsy for BSs/PCSs was graded lower by LMIC respondents ($60.9 \pm 34.5\%$, $n = 22$) than by UMIC ($79.8 \pm 30.9\%$, $n = 55$) or HIC respondents ($76.9 \pm 28.4\%$, $n = 196$), although almost all respondents would recommend or attend it (*Questions 21 and 22*). In *Question 23*, most respondents favored the continuous online programs (LMIC 55%, UMIC 54%, HIC 47%) or the brief (≤2 weeks) in-presence training (LMIC 62%, UMIC 49%, HIC 58%) and country income designation had no significant effect (nominal logistic fit). However, the long (1 month) in-presence training format was more appealing among LMIC (38%) or UMIC (38%) respondents than HIC respondents (16%; nominal logistic fit, $p < .001$), even though this was the least-preferred option (significant difference in preference only for HIC respondents, Pearson $p < .001$). Almost all respondents to *Question 24* (97%) favored ILAE involvement, with the highest preference for regional **coordination** (LMIC 45.5%, UMIC 55.4%, and HIC 34.2%; nominal logistic fit, $p = .0168$; UMIC vs HIC OR, $p = .005$).

4 | DISCUSSION

The main findings that emerged from the survey are the following: (i) most respondents across all categories were engaged in preclinical studies, with the highest engagement among PCSs and lowest among CSs; (ii) broad understanding of both clinical and neurobiological aspects of epilepsy was reported by 48% BSs/PCSs; (iii) the large majority of respondents declared an interest in clinical issues; (iv) more than half of BC/PCS respondents regularly or often interacted with epileptologists; (v) training activity on clinical aspects dedicated and customized for BSs/

PCSs was considered recommendable by 81% of the participants in the format of 1–2 week in-presence tutoring or as continuous online training; (vi) gaps in understanding preclinical research and neurobiology aspects of epilepsy were more pronounced among CS and LMIC respondents. To highlight BS/PCS opinion on training organization, the last survey questions were focused as binary options, even if this could lead to acquiescence bias.

The survey suggested broad interest from BSs and PCSs on the five continents. We asked whether the 237 survey respondents are representative of the BSs/PCSs working on epilepsy, measured by counting the number of attendees qualified as either BSs or PCSs at recent international epilepsy congresses, such as the 2023 ILAE Conference (373 attendants) and the 2022 European Congress on Epilepsy (257 attendants). We extrapolate that the participants recruited for our training questionnaire are likely to represent BSs and PCSs who are active in the field of epilepsy attending the major international epilepsy conferences. Because the survey distribution was disseminated mainly through the ILAE website or ILAE-derived special groups, we are confident that a representative portion of active BSs/PSCs attending international epilepsy congresses was consulted. The number of BSs and PCSs presenting data is usually larger at local national meetings: for example, 247 BSs attended the 2023 American Epilepsy Society meeting (13% of these from outside the United States), and the annual meeting organized by the Neurobiology Commission of the Italian League Against Epilepsy gathered 76 BS participants. Of interest, 32 and 29 survey respondents were counted in the United States and Italy, respectively, suggesting that the survey penetrance among active BSs/PCSs working in epilepsy was uneven across nations and regions. The regional distribution of the responders demonstrated a limited representation from regions outside Europe and North America. A language bias due to the fact that the questionnaire was in English could have limited the number of respondents from not native-speaking English countries. When the number of basic scientists attending the ILAE international meetings of 2022 and 2023 was analyzed, we observed a similar continent distribution. This difference in the representativeness of BS/PSC respondents in different nations represents a limitation of the present report that could be resolved in the future by running the survey at the level of national ILAE Chapters. Moreover, it is worth mentioning that scientists working in epilepsy may not be involved in ILAE Congresses; it would be interesting to disseminate the present survey at meetings of neuroscience societies unaffiliated with the ILAE, to broaden the value of the observed findings.

Despite the relatively broad participation in the survey, some subgroups/categories were less represented than others; this represented one of the significant limitations of the present report. Demographic features of the recruited population were homogeneously distributed in terms of gender, age, working environment (non-university vs university), and self-assigned BS vs PCS role. Uneven, but well-represented, groups were identified for the working position category, which covered roles ranging from MD/PhD student to senior scientist/faculty. A small group of respondents working in private environments was recruited; this group was crucial to compare the opinions generated in the industrial environment to those in public/academic research settings. The geographical distribution of the respondents was the most asymmetrical category. European scientists represented 45% of the participants, whereas applicants from Africa, Asia, Oceania, and Eastern Mediterranean countries were less represented. To facilitate the analysis of the responses derived from different geographical areas, we merged respondents from countries according to the World Bank income rating, assuming a homogeneous point of view from income-alike regions.

This report gives a broad and plain description of the main elements emerging from the survey. The analysis of the responses reported in the Results did not focus on specific multivariate evaluations—except for responses to *Question 19*, which were highly heterogeneous among categories. More detailed analysis of responses will still be possible in the future to better understand specific issues raised by the questionnaire.

Responses to *Questions 8–20* of the different groups that deviated from the overall opinion are summarized here. Among those respondents identified as BSs and/or PCSs, male respondents were more frequently involved in preclinical work than female respondents. BSs perceived the clinical epilepsy terminology language barrier as one of the elements interfering with the interaction with clinicians, and considered clinicians not much interested in the neurobiology of epilepsy. A lower number of LMIC respondents declared competence in both clinical and basic epilepsy and were more inclined to perceive epilepsy mainly as an issue of hyperexcitability. MD/PhD students declared that time availability and language gap as crucial limiting factors for the collaboration with clinicians and perceived that clinicians are not interested in collaborating with basic scientists; moreover, MD/PhD and postdoctoral fellows found the information gathered during epilepsy congresses was not especially relevant for their daily working activities. A large number of senior scientists are involved in collaborative projects with clinicians who fund their research activity and have a better-than-average understanding of both clinical and basic epileptology. Concerning the working environment, scientists working in industry (i) performed more often

than average preclinical studies, (ii) were less interested in publishing their results and in receiving a grant to fund their research, (iii) declared above-average understanding of both clinical and basic aspects of epilepsy, and (iv) were more keen than other groups to participate in epilepsy congresses.

Clinical training dedicated to BSs/PSCs was less relevant for MD/PhD students and LMIC respondents. Younger researchers preferred on-line to in-person training, and the opposite trend was prevalent among researchers working in private companies. LMICs preferred long-term training organized at the regional level. A limitation of the present survey that may restrict the conclusions was the lack of response of members of several ILAE chapters. Two conditions can explain this situation. One is the diverse distribution of the survey among the different chapters. Another possibility is the lack of presence of BS/PCS in several countries included in the LMIC category. This last situation should be considered for future surveys to promote basic research in different regions of the world.

Although we based our questionnaire on an a priori concept of BS vs PCS, the survey responses revealed that preclinical and translational research is being conducted by a diverse group of investigators, not necessarily defined by the level of self-perception as PCSs. Initiatives that target preclinical or translational research issues should, therefore, be directed to the broader scientific community to reach interested investigators. Of interest, CSs were less likely to perform preclinical research for reasons that were beyond the scope of our survey. Although this could be due partly to preference toward clinical research or lack of qualification for preclinical models, future surveys could explore whether modifiable factors are also involved, that is, opportunity for collaborations with PCSs/BSs, occupational firewalls, training, and funding. Of interest, CSs admitted a suboptimal understanding of preclinical research and of neurobiological aspects of epilepsy, highlighted by the perception that most thought that epilepsy is a straightforward condition of enhanced excitability. Educational opportunities to target CSs and improve their understanding of preclinical and basic science research would fill a gap in future endeavors and facilitate more two-way interaction collaborations across research arenas.

Our survey demonstrated some gaps in regard to lower resource countries. Greater representation of CSs was noted among the respondents from UMICs, LMICs, and LICs, although the LIC was under-represented in our survey. Initiatives to further explore how best to develop preclinical research opportunities in non-HICs through collaborations and training would be worth considering. The clinical-oriented educational program targeting BSs/PCSs was well received across groups, with a strong preference for involving ILAE and regional/national coordination, underscoring the region- and country-specific factors that need to be considered in this effort.

The survey explored an area wider than epilepsy research and touched on aspects broadly related to translational research. Some of the conclusions could be exported to other areas of neurology and to the relationship between basic science and clinical environments at large. A specific strategy for solving the identified issues has been developed within the ILAE Neurobiology Commission; a set of guidelines for training program modules dedicated to basic researchers working in epilepsy have been developed and are under validation. These training modules could be adopted by different centers at the international and regional levels and could be exported, in principle, to other areas of neurology/neuroscience and medicine.

5 | CONCLUSIONS

The survey revealed some novel and important insights that could help develop approaches to bridge the gap between treating clinicians and those who identify themselves as BSs/PCSs. Both sectors are critical to optimize care for people with epilepsy but research by either party will be irrelevant without the capacity to translate and transition. To enable the best outcomes all stakeholders should engage and develop research concepts aiming for an optimal translation of bench-to-clinic outcomes. The next stage is to develop accessible resources to ensure uptake of clinical epileptology language by BSs/PCSs, and similarly that critical neurobiology concepts are included in clinical training curricula, as recently expressed by a survey on educational need of a young community of epileptologists organized by the Italian Young Epileptologist Section of the ILAE.[3]

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CONFLICT OF INTEREST STATEMENT

This report was written by experts selected by the International League Against Epilepsy (ILAE) and was approved for publication by the ILAE. Opinions expressed by the authors, however, do not necessarily represent the policy or position of the ILAE.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

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

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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