

Meeting report International Scientific Advisory Committee (ISAC) April 22-23, 2022 (Meer en Bosch, Heemstede, Netherlands)

Introduction

ISAC's main task is to review and analyze the progress of scientific research in SEIN and to give suggestions for further improvement.

Recently, two new members joined ISAC: Anna Jansen, pediatric neurologist from Bruxelles (Belgium), expert on epilepsy genetics, and Claudio Bassetti, neurologist from Bern (Switzerland), famous sleep researcher.

Anna Jansen could join the present meeting online; Claudio Bassetti was not able to attend.

Participants

Stichting Epilepsie Instellingen Nederland (SEIN): Eleonora Aronica, Tirza van Hal (management assistant), Gert Jan Lammers, Stiliyan Kalitzin, Ley Sander (director of Scientific Research), Roland Thijs, Gerhard Visser, Maeike Zijlmans, Renate van Regteren, Femke van 't Hof, Silvano Gefferie, Robert Helling.

Board of supervision: Monique Bensen-Lemmers (chair), Elles Tromp, Jaap van Rhijn, Frank van der Linden, Ruurd Jan Roorda.

ISAC: Anna Jansen (Bruxelles, online), Martin Holtkamp (Berlin), Eugen Trinkla (Salzburg), Oebo Brouwer (Groningen, chair). Notice of absence from Claudio Bassetti (Bern).

Programme

Ley Sander welcomed all participants and gave an overview of recent SEIN research.

Presentations on the latest research topics were then given by Silvano Gefferie and Robert Helling (PhD students, TMS), Lammers (sleep), van Regteren (drug withdrawal strategies in epilepsy), Zijlmans (invasive investigations in epilepsy), Thijs (implementation of seizure detection devices in epilepsy), Aronica (identification of druggable targets from transcriptome datasets for epilepsy of structural etiology) and van 't Hof (future of genetic research).

Roland Thijs then presented a concise overview of the strategic research plan (see next paragraph). This was followed by a lively discussion with some issues emerging. Considered most important is what for SEIN and its research would be the best way to proceed. First option was to arrange a closer partnership with Leiden University Medical Centre. Second, to do the same with a foreign university. Third, to continue its present 'stand alone' position. Another issue discussed was the generally felt urge to improve public relations and disseminate main themes of research and the results in a better way both to the general public and the staff members of SEIN not directly involved in research.

Ley Sander closed the session.

'Research Strategy SEIN 2022-2027'

Key statement is the paradigm shift moving from usual trial-and-error treatments to *targeted personalized approaches*.

SWOT analysis

- strengths: leading research lines e.g. epilepsy surgery, SUDEP & seizure detection, neuropathology, narcolepsy; research funds from Christian Society; excellent infrastructure.

- weaknesses: minimal institutional support; lack of academic infrastructure, only partly supplied by SEIN; no systemic recording clinical data; limited media exposure for research projects.
- opportunities: CASTOR becoming standard as research database; European Reference Networks offering coordinated approach for rare and complex disorders.
- threats: no allocation of grants to non-academic institutions like SEIN; increasingly complex research regulations requiring more staffing.

Strategic direction

Redefine research priorities to catalyse *personalised treatments*:

- innovative technologies to elucidate epileptic networks and those involved in sleep pathology;
- genomics and deep phenotyping;
- improving monitoring at home.

Strategic goals and requirements

Providing *precision personalised care* enabling every person to have effective treatment at the earliest opportunity.

This can only be accomplished by full cooperation of SEIN, LUMC and UMCU in a shared vision, and with other centres and institutions abroad (UCL), and by significant capital investment: expanding and intensifying collaborative networks; maximising research output; investing in clinical database structure; investing in research governance and management; and increasing visibility and impact.

Scientific achievements (PhD's, output, external funding)

- PhD's: 2020: 5; 2021: 2; 2022: 3 (planned).
- list of publications: 2020: 105; 2021: 99; 2022: 26 (until April 4). Papers were categorized according to research programmes: I. Paroxysmal disorders and comorbidity; II. Refractory epilepsy; III. Translational research. For 2021 the programme Sleep had been added.
- external funding: 2020: 3118 k€; 2021: 3101 k€; 2022: 1588 k€ (including 1166 k€/year from the Christian Society).

Analysis

Scientific research in SEIN has made steady progress over the last two years. The numbers of project funding, scientific output and PhD theses are quite impressive.

A further look at the *project funding* shows a clear overlap over the years 2020-2022. Of the full 3-year period amount of 5450k€, the Christian Society funding part is 3498k€ (1166k€/year) (64%) and the external funding part 1952k€ (36%).

The Christian Society funding is mainly used to finance the chairs of Aronica (UvA, one day/wk), Lammers (LUMC, two days/wk) and Zijlmans (UMCU, one day/wk), the position of Thijs (two days/wk), and some PhDs.

The *scientific output* of 204 papers in 2020 and 2021 combined, is generally of high quality with many papers in high ranked journals. First or last authorship can be identified in 81 (40%) papers. In 167 (82%) only one author from SEIN is involved, most often Sander (56 papers) and Aronica (46 papers). Categorising of papers was in accordance with original research programmes. Remarkably, 34 (17%) papers did not concern paroxysmal disorders, but other subjects from pediatric or general neurology (for instance general movements in young children or adult oncology). In 2021 a category sleep was introduced, but many papers dealing with sleep were still included in other categories.

In 2020, four *PhD theses* were completed, and two in 2021. In some of them the connection with SEIN research was unclear. The PhD thesis of Amerins Weijenberg, for example, who during part of her research period worked as a child neurologist in SEIN (Zwolle), was done at UMCG (Groningen) without any connection with SEIN research.

Most high quality research is done by a few PIs, in part in collaboration with PhD students. The majority of clinical working neurologists and neurophysiologists at SEIN are not involved in research which can be deducted from the listed scientific output.

Compliance with regulatory requirements is good and no issues were identified. The back office is very efficient in keeping track of all the ongoing projects.

The issue most extensively discussed during the Friday afternoon session, and also the next morning during a separate meeting of ISAC members with Ley Sander, is how SEIN research can keep up its high standards for the years to come. It seems obvious that close collaboration with a university is the best way to be able to attract more PhD students, get easier access to external funding and library facilities, and to facilitate interaction between research groups. For several reasons the most obvious candidate would be Leiden University Medical Centre.

A great challenge is how to keep SEIN's own identity visible within combined research efforts. An important step forward is defining the delivery of '*precision personalised care*' as a major strategic goal. Consequently, research priorities have been redefined and include mapping brain networks, deep phenotyping and developing home monitoring devices for seizures and sleep disorders.

Another important step forward are the recent developments in integrating research of Kempenhaeghe and SEIN.

Conclusion

SEIN is an expertise centre for epilepsy and sleep medicine with a scientific performance that has been successful in the last two years. Its vision on research has been recently restated as based on moving from usual trial-and-error treatments to *targeted personalized approaches*. For SEIN as a stand alone research institution the greatest challenge is to create a research partnership with an university medical centre for several reasons.

Suggestions

The future of scientific research in SEIN heavily depends on strategic choices the institution is going to make with respect to engaging strategic alliances with one of the universities and with Kempenhaeghe.

Apart from that, further focus on the recently redefined research priorities within the theme '*precision personalised care*' is needed. It is important to share this with all SEIN employees but also to the general public and colleagues working in the field of epilepsy and sleep.

Reporting on scientific achievements might be more clearly connected with the newly formulated research lines (innovative technologies to elucidate epileptic networks and those involved in sleep pathology; genomics and deep phenotyping; improving monitoring at home). Research outside these research lines should be categorized separately. Besides impact factors, Q-indexes (Q1-Q4) might be added to the publications listed.

Performing research involving more clinicians/staff members from SEIN apart from the PI's demonstrated by more multi-authorship publications should be encouraged.

Apart from scientific output, reporting direct effects of ongoing research on daily patient care should be considered.

It had been agreed to organize the regular meetings of ISAC with the researchers of SEIN biannually and to have a paper audit in the years in between.

Due to the recent Covid pandemic the originally planned schedule had to be adapted. The next ISAC meeting is now foreseen in October 2023, with arrival of committee members on Thursday evening, meetings on Friday and Saturday morning, and departure on Saturday afternoon. Candidate dates should be proposed as early as possible.

It was recently discussed that the review process should preferably also include interviews with the Board of supervision/Board of directors and with a representative from the involved university.

The members of the International Scientific Advisory Board,

Anna Jansen
Martin Holtkamp
Eugen Trinkla
Oebo Brouwer, chair

Bruxelles/Berlin/Salzburg/Groningen, June 29, 2022