



Evaluation report for the research review of

## **Amsterdam Neuroscience**

for the period 2016-2021

Research review according to the  
Strategy Evaluation protocol 2021-2027

May 2023



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This report was finalized on 2 May 2023

## Preface

I am happy to present to you the evaluation report based on the research review of Amsterdam Neuroscience for the period 2016-2021, conducted on-site September 27-29, 2022. It was a true pleasure to meet so many engaged neuroscientists, and to review such a prestigious program. I have had the opportunity to follow the progress of Neuroscience Amsterdam and it truly serves as an international role model. The on-site review was carefully planned in any detail, and a great overview of its activities were provided for us to read beforehand. Thank you to Arjen Brussaard and colleagues for being such great hosts and providing such a nice and well-organized environment.

I also want to sincerely thank my colleagues on the review panel, co-chair Prof. dr. Elisabeth Binder, Prof. dr. Berry Kremer, Prof. dr. Patrik Verstreken, Dr. Aldo Jongejan, Drs. Merel Heimens Visser, Lianne Hulshof MSc for making up such a great and diverse team. It was truly a pleasure to work with you! Also thank you to Dr. Meg van Bogaert to keep us on track and to help put together this report.

On behalf of the entire review board, we hope that you will find the report useful, and we wish you good luck with your important work also in the future.

**Professor Gitte Moos Knudsen**  
**Committee chair**  
**November 2022**



# I. Introduction

## Scope of the assessment

The Executive Boards of the Vrije Universiteit Amsterdam and the University of Amsterdam commissioned a review of the research conducted at Amsterdam Neuroscience. The review is part of the regular six-year quality assurance cycle of the university; it is intended to monitor and improve the quality of the research and fulfil the duty of accountability towards government and society. The quality assessment in this report is based on the assessment system in the Strategy Evaluation Protocol for Public Research Organizations 2021-2027 (SEP, appendix 1), drawn up by the Universities of the Netherlands, the Netherlands Organization for Scientific Research (NWO) and the Royal Netherlands Academy of Arts and Sciences (KNAW).

## The review committee

The Executive Boards of Vrije Universiteit Amsterdam and University of Amsterdam appointed a review committee (hereafter: committee) of external peers, including a mid-career researcher, a (recently graduated) PhD candidate and a representative from industry. The committee consisted of:

- Prof. dr. Gitte Moos Knudsen (chair), University of Copenhagen, Denmark;
- Prof. dr. Elisabeth Binder, Max Planck Institute of Psychiatry, Germany;
- Prof. dr. Berry Kremer, University Medical Center Groningen, the Netherlands;
- Prof. dr. Patrik Verstreken, VIB-KU Leuven, Belgium;
- Dr. Aldo Jongejan, Amsterdam University Medical Center, the Netherlands;
- Drs. Merel Heimens Visser MBA, Director Brain Foundation, the Netherlands;
- Lianne Hulshof MSc, University Medical Center Utrecht, the Netherlands.

Dr. Meg van Bogaert was appointed as independent secretary to the committee. Members of the committee signed a declaration

and disclosure form to the effect that they would judge without bias, personal preference, or personal interest, and their judgment would be made without undue influence from the institute, programs, or other stakeholders. Any existing professional relationships between committee members and programs under review were disclosed. The committee concluded that there was no risk in terms of bias or undue influence.

## Assessment criteria

The Strategy Evaluation Protocol 2021-2027 ('SEP') was the starting point for the committee's review. This protocol describes the aims and methods used to assess publicly funded research in the Netherlands.



SEP 2021-2027 identifies three main assessment criteria: (1) research quality, (2) relevance to society and (3) viability. Furthermore, SEP asks committees to take four specific aspects into account when assessing the three central criteria. These are: (1) Open Science, (2) PhD Policy and Training, (3) Academic Culture and (4) Human Resources Policy.

In addition to the guidelines and criteria suggested by the Strategy Evaluation Protocol, the committee considered the Terms of Reference issued by the Executive Boards of the universities.

## Documentation

The committee received detailed documentation consisting of:

- Self-evaluation reports 2015-2020, including appendices;
- Strategy Evaluation Protocol 2021-2027;
- Documents related to the *sectorplan*.

## Working method

The site visit took place in Amsterdam on 28 and 29 September. Before the site visit, the committee members were asked to read the documents provided above and formulate topics for discussion and questions for the interviews. At the start of the site visit the committee discussed its preliminary findings.

During the site visit, the committee met with representatives of the university, institute and programs and discussed its findings. To conclude

the site visit, the committee chair presented the main preliminary conclusions. The schedule for the site visit is included in appendix 2.

At the end of the site visit, the committee members formulated their findings and drafted a first version of the report. After the site visit, the secretary drafted a complete version of the committee report, based on the input drawn up by the committee members. It describes the findings, conclusions, and recommendations of the committee. This draft report was circulated to the committee for all members to comment on. Subsequently, the draft report was presented to the participating universities for factual corrections and comments. After considering this feedback in close consultation with the chair and other committee members, the secretary finalized the report. The final report was presented to the Executive Boards of the universities and the board of Amsterdam Neuroscience. The report was completed on 2 May 2022.

## II. Amsterdam Neuroscience

### 2.1. Introduction

The Amsterdam Neuroscience Institute was founded in 2016 as an interdisciplinary collaboration of Amsterdam UMC and the science faculties of the Vrije Universiteit Amsterdam and the University of Amsterdam. It is one of Amsterdam UMC's eight research institutes and has nearly 800 participants / scientists. One of the aims of the Amsterdam Neuroscience Institute is to bridge the gap between basic research and clinical medicine by gaining an understanding of various brain disease mechanisms.

The committee was charged with looking at the Amsterdam Neuroscience Institute but noticed that there is room for improvement when it comes to communication and interaction with the other institutes of Amsterdam UMC. Given that some facilities are shared and are not only used by Amsterdam Neuroscience, even more interaction *between* the institutes, e.g., oncology, could be an advantage. This could be brought to the Amsterdam Research Board. By strengthening mutual interaction, institutes can learn from each other and act together to address cross-institute challenges.

### 2.2. Governance and strategy

#### 2.2.1. Organizational structure

Amsterdam Neuroscience has organized its research along nine translational research programs, each around a specific brain and nervous system disease, disease mechanism or technology innovation. Five of the initial research programs focus on specific brain and nervous system diseases, and four programs focus on innovation and technology. The nine programs are organized in a matrix. Each of the programs has a dedicated steering committee and includes – on average – 25 Principal Investigators (PIs). A midterm review in 2019 led to an internal SWOT and restructuring of the organization.

Amsterdam Neuroscience is an interdisciplinary collaboration of Amsterdam UMC and the science

faculties of the Vrije Universiteit Amsterdam and the University of Amsterdam. Of the nearly 800 participants in the institute, 75% is appointed at the Amsterdam UMC, and 25% is affiliated with the science faculties of the two universities. Combining the strengths of the various organizations is a great endeavor. All programs include scientists from the different organizations and scientists from those organizations also seem to meet each other in many programs. However, dealing with these different organizations in one institute presents challenges. The fact that scientists are assigned to different organizations obfuscates transparency when it comes to overhead costs, for instance. These costs seem to vary between the organizations, creating differences between and within programs. Ideally, such overhead costs would be comparable between organizations, but the committee understands that this is not an easy task. It therefore advocates transparency.

Communication is a focus point of the new directors. The committee supports this vision, regarding both communication among programs and between institute leadership and programs. There is a lot of potential for more collaboration among research programs, which could also provide new opportunities for joint grant funding. The annual meeting is a very important point of exchange and communication but is not sufficient to establish viable connections. In addition to the leaders from the different programs arranging meetings, dedicated online communication platforms may facilitate exchange of relevant information and views. Within the institute and within specific programs, there is a lot of knowledge, e.g., on technologies, that other members of the institute are not aware of. The director highlighted that information about available resources and technologies could be easily spread via existing webinars that are recorded and by establishing online exchange fora. By improving communication, the institute can enable interaction and sharing of knowledge, including knowledge beneficial to infrastructural groups. This is particularly important for young



scientists who are still in the process of building up a network.

The committee would even suggest taking communication one step further and work on improving external communication. A great institute like Amsterdam Neuroscience could and should create much more awareness about what they do, showing it to the world. In one of the meetings, it was mentioned that small improvements might already have impact. For example, the location of the website makes it difficult for external parties to locate and position the institute. The committee proposes that the leadership of the institute considers expanding its connections to national and international organizations, such as the newly established European infrastructure EBRAINS.

### *2.2.2. Mission and strategy*

The overall mission of Amsterdam Neuroscience is to broaden the fundamental knowledge about the (central) nervous system and to translate this into effective therapies and treatments for individual patients with a neurological or psychiatric disorder. The interdisciplinary research institute aims at making a powerful impact in the field of basic and translational neuroscience. Furthermore, it aims at being a breeding ground for the next generation of neuroscientists.

Amsterdam Neuroscience focusses on scientific excellence, young talent, and innovation in four cross-disciplinary research programs. In addition, there are five clinical-oriented research programs that focus on existing and novel treatments for a number of brain and nervous system diseases. In 2019 Amsterdam Neuroscience introduced the slogan: Connecting the people, the science, and the brain. Seven major strategic points of attention were formulated to reach a wider community of stakeholders.

## **2.3. Quality of the research**

Overall, the committee was very impressed by the excellence of the research programs within Amsterdam Neuroscience. Already since its start the institute stood out with respect to the quality

of its work, and it has further developed over the years into a strong research institute. The scientists in the nine research programs all recognize the importance of Amsterdam Neuroscience. Despite being involved and busy with their own research in their own departments, they state that Amsterdam Neuroscience clearly brings added value to their work. In Chapter 3, the committee provides an in-depth evaluation of the nine programs of Amsterdam Neuroscience.

A major catalyst for the added value of Amsterdam Neuroscience was its seed funding initiative. The relatively small amounts of funding provided to selected researchers and groups have proven to be extremely important for gluing together the - sometimes - diverse groups in the programs. For example, by providing some seed funding the very strong Alzheimer and Parkinson groups started to collaborate. The committee is of the opinion that the intention of Amsterdam Neuroscience to stimulate collaborations, was successful. It achieved a lot with relatively little money.

Many programs applauded the Amsterdam Neuroscience business development office. This so-called Industry Alliance Office (IAO) was set up to bridge the gap between academia, medical faculty, hospitals and the biotech and pharma industries. Scientists from multiple programs indicated that the IAO functions very well and, on many occasions, played a pivotal role in connecting research to industry. More information about the committee findings on IAO is provided in Chapter 2.4.

### *2.3.1. Funding*

The outstanding quality of the research is, among other things, reflected in the high levels of external funding. For some programs this external funding reaches or even exceeds 90% of the total program budget. Impressive as it is, it also makes these programs vulnerable. Many scientists are hired on external funding which usually means temporary contracts. This is common for many scientists worldwide, but there is a tipping point where the external funding constitutes a

disproportionate part of the funding. This imbalance may imperil a program's viability. Uncertainty about a future as a scientist, due to temporary contracts, may lead to departure of talent. Changes in national or international funding policies may quickly downgrade a successful program. Furthermore, keeping infrastructure in place, including highly skilled support staff, is highly relevant to the future success of the institute. Failing to do so, even for a brief while, will make rebuilding such infrastructure difficult.

The committee is fully aware of the fact that much of the funding for research lies with the departments at the organizations employing the scientists. Amsterdam Neuroscience itself has a limited amount of structural funding. Wanting to see Amsterdam Neuroscience flourish even more in the upcoming period, the committee advises the new leadership to address this issue of structural and secure funding.

### 2.3.2. Facilities

Shared facilities were discussed extensively during the site visit. The committee is aware of the fact that issues concerning shared facilities are not unique to Amsterdam Neuroscience, nor to its parent organizations. Nevertheless, the committee emphasizes the importance of considering how to organize access to – for example – biobanking and computing storage and capacity. Options are to remain the current situation of distributed systems, or all programs – and the institute as a whole – could benefit from a more centralized organization and support.

Animal facilities are a specific challenge for scientists at Amsterdam Neuroscience. The committee discussed with participants from several programs how to deal with the public perception of animal research. The committee appreciates the outreach by the institute leadership to the local population, which is incredibly important. It shows that the institute understands that interaction with population is important to clarify why animal experiments are sometimes unavoidable despite the public opinion.

Animal research is important to the programs, and the committee recommends the leadership of these programs to take on an active role, together with the Amsterdam Neuroscience leadership, to advocate for animal research both at the highest level of policy making in the Netherlands, *and* together with other EU neuroscience institutes at EC level.

### 2.3.3. Open science and data

As the Amsterdam Neuroscience is a network institute, the research programs are physically located at different sites across Amsterdam. These sites each have their own data storage facilities and computational infrastructure. At these local levels, new initiatives are deployed to adhere to the Open Science policies. The importance of adhering to FAIR principles is increasingly being recognized and money is allocated to install dedicated Data Stewards at the various Core Facilities.

Within Amsterdam Neuroscience institute, the research programs have unanimously expressed a need for better data storage facilities, better data sharing and more computationally trained people to perform the increasing number of data analyses. The committee recommends a strategy for supporting AI, not only by hiring high-level senior staff (professors) but also by hiring data assistants and programmers. This will require tenure-track positions in the field of complex data analyses as well as support personnel to curate data, secure data quality and perform analyses as a service. This is not easily done with external funding, because AI capabilities requires a solid core facility. In addition to the hardware component, data must be stored safely, with adequate quality assurance, while data storage should be standardized. The existence of or access to a shared data storage facility could benefit the coherence of Amsterdam Neuroscience institute.

In addition to data storage, the committee discussed data sharing. Many scientists in several programs are keen on data sharing, but often struggle with regulations. GDPR limits data sharing opportunities. Especially for large multi-center cohort studies it is often difficult to share all data.

It was mentioned on multiple occasions during the site visit that the legal office is too slow in helping, in virtually all aspects where their help is needed.

## 2.4. Valorization and impact

### 2.4.1. Industry Alliance Office

Translational neuroscience is at the core of the collaboration between university labs, clinical practice and the biotech and pharma industries. Support to provide the gap between academia, medical faculty, hospitals, and industries is provided by the Industry Alliance Office (IAO). IAO acts on behalf of the entire Amsterdam Neuroscience Institute. The IAO team supports both translational neuroscience contract research and clinical trials. They form a one-stop-shop for biotech and pharma industry for fast contracting of basic and translational science. The amount of IAO supported grants has reached a substantial value of € 57.2 million as part of the institute's valorization strategy.

Part of the success is the enrolment of specialized businesses developers who interact with industry and research programs. The intensity of using IAO by different programs differs. The committee noticed that some could benefit more from IAO services. The use of IAO may be stimulated across the institute by increasing awareness and sharing success stories. Nevertheless, the overall appreciation of the IAO services is very high. Many programs mentioned to be impressed by the services offered. The IAO seed funding initiative helped kickstart new cooperations in and between the research programs.

Despite strong appreciation within the institute of IAO, the committee identified a problem regarding overhead. Some projects face up to 75% combined overhead on projects funded by charity organizations and Pharma sponsored trials. This not only limits the chances of getting funding for a project but also misses out a meaningful way to interact with society and act upon societal needs. A number of programs proposed a broadening of the IAO services, including e.g., the advocacy for neuroscience topics in national political arena's

(e.g., on animal research). The committee recommends keeping the strengths of IAO intact and showcase internally the benefits of IAO.

### 2.4.2. Stakeholder involvement

In addition to valorization and impact, Neuroscience Amsterdam engages in outreach activities. The different research programs vary in their stakeholder involvement (e.g., patient groups) in the preparation and execution of their research strategy. In several cases the committee has observed a knowledge push rather than patient/societal involvement. There also appears to be a lack of evidence-based influence of the research on society. The committee is of the opinion that by formulating more precisely what Amsterdam Neuroscience considers societal relevance, the institute can not only inform the public but also should attract and involve patients and other stakeholders in the development phase of the research projects. This is also increasingly done by industry, ensuring that people adhere better to trials and studies. For Amsterdam Neuroscience, this could help identify future research opportunities. The institute should consider whether it might play a role in advocating on a national level and assist programs in societal interaction to align societal needs with research strategy

Communication on the website and in the magazine is often in English with an academic language. By making the website neutral and more accessible, and developing a magazine for the lay audience even more outreach can be achieved.

### 2.4.1. Legal aspects

Several programs identified legal issues as a bottleneck. In fact, the committee received many complaints about how legal departments are strongly protective of the organization's interest in case of contract negotiation. This impairs industrial interactions, because for potential industrial partners the process of getting negotiations started will be too cumbersome. They will move on to other organizations for faster negotiation-tracks.

The review committee recommends improving the functioning and speed of the legal departments' processes, to reduce workload for the scientists and decrease bureaucracy. Funding contracts, progress reports, starting trials, or documenting travel costs are very time-consuming. Improvements in such procedures are essential for scientists to devote more time to their core work. The legal departments of the two academic hospitals appear to be in a process of merging. It is crucial to improve transparency about this process and how long this will take. Input and directions from researchers as to what is needed would benefit the future legal organization. Another opportunity worth looking into is outsourcing of these legal issues. This has been done before, apparently with good results.

GDPR is a challenge for the programs, prohibiting open science. The institute is clearly aiming – and according to the committee has an obligation – at stimulating open science. But to deal with this it requires 1) legal support and 2) computational support. The committee emphasizes the importance for the organizations and their legal departments to find a balance between protecting the hospital and universities from legal missteps and performing open science. The committee emphasizes to the leadership of the Amsterdam organizations that it is important to scientists that legal support does not always shy away from any grey zones. This issue is not limited to Amsterdam Neuroscience and the solution is also largely outside the institute's hands. The committee nevertheless encourages the leadership to raise this issue with the relevant organizations.

## 2.5. Future strategy

In the month after the site visit (October 2022) the new directors took over the leadership of the institute. In the meeting of the new directors with the committee several major strategic issues were discussed. The directors identified areas that need attention. Although the challenges in these areas are not easily solved, and require many years of incremental changes, it is essential to try and identify the core of these problems and formulate a vision, as well as aims and strategy. The mere

acknowledgement of such problems will signal to the different research programs attention for these issues attempts to address them.

For one, the new directors have spoken with all programs to evaluate their relationship with Amsterdam Neuroscience. In alignment with the impressions of the committee, the new board of director also noted quite a spread in the intensity of involvement of the different programs in the institute. The directors plan to improve involvement by working with all programs to raise awareness about the potential benefits of being part of Amsterdam Neuroscience. This will be done by highlighting success stories, for example how research support from a company could be secured, starting at initial basic research findings, and continuing to the clinical trial, thus involving and benefiting several groups and programs. The new directors feel that this is especially pertinent for PIs who are not working at Amsterdam UMC, but at the Science Faculties of VU and UvA.

The directors also appreciate the relevance and importance of funding, part of which could support directly or indirectly benefit Amsterdam Neuroscience. This is possible within major national grant programs but is dependent on specific calls. The directors highlighted possibilities of obtaining additional funding for the Institute by interacting with pharma-companies that could be offered access to facilities as well as the benefit of negotiating with a single partner. In fact, income from the valorization initiative has already been used as seed money for the Proof-of-Concept studies.

The directors also acknowledge as a major issue the increasing bureaucracy for animal research and the ever increasing and often non-transparent increases in overhead, especially when acquiring international or private grants. In addition to the issues that were identified - and are being worked on – by the new directors, the committee has several issues it would like to point out for the upcoming years.

The committee is positive about the bench-to-bed strategy and thinks it is important that all

programs have their position in this strategy, but every program does not necessarily have to cover the entire bench-to-bed scope. Some programs clearly fit in the translational strategy, for other programs this is less obvious. The committee recommends that all programs are aware of the Institute's strategy and subsequently relate this strategy in their own program. To be successful in the overall institute strategy, support and leverage from all programs is essential.

The committee noticed that the strategy up until now was inward looking. Reflection on how to interact not only within the programs but also with the Amsterdam UMC, the two faculties involved, other university institutes, and with outside parties (NIN, other universities, NWO / ZonMW and even relevant ministries) should be emphasized in the future strategy.

Although the committee is somewhat hesitant to stimulate Neuroscience Amsterdam to further broaden its scope, it suggests considering including new areas, e.g., AI and Psychology. Reaching out to and interacting with university departments might result in shared positions. A lot of expertise will find its way to the hospital.

## 2.6. Academic culture and HR

### 2.6.1. *Team science*

The institute strives to facilitate team science, which is considered of significant importance in, for example, translational research. In this respect, Amsterdam Neuroscience enhances an open academic culture. This is also what the committee observed: a good atmosphere, with an open culture. As part of the ambition to have a flourishing academic culture the institute plays an active role in communication. Staff members much appreciate the institute's yearly meeting. It showcases research, is an event to inspire and connect the research communities. The forming and feeding of this network are important prerequisites for the ambitions around team science.

The lab help email-address is an outstanding example of a simple yet elegant tool to tap into

the knowledge shared across the institute, and to quickly connect people across different research groups.

Numbers show an increasing appetite for the various communication products. The yearly magazine, website, LinkedIn, and Twitter are aimed at a professional target group. In the next phase it would be beneficial to add the general public as a target group to enhance support for neuroscience.

### 2.6.2. *Diversity and inclusivity:*

Diversity is not only about gender but should be more widely adopted. For the committee it was difficult to assess policies concerning diversity and inclusivity, since the institute does not hire the scientific staff. Nevertheless, in a more informal manner Amsterdam Neuroscience can work on diversity and inclusion. For example, the mid-career scientists who do not master Dutch told the committee that they sometimes encounter hurdles when joining institute or program meetings. Often these meetings are in Dutch, and they feel excluded, being the only non-Dutch speaker. Issues like this are easy to overcome but require a conscious policy about the language used in meetings.

The gender balance is such that more senior and higher positions are taken up by men, while the younger generation often predominantly consists of women. Hopefully over time more women will occupy senior positions but the committee recommends a more proactive approach to maintain, at the very least, the variety of initiatives that are already in place.

Diversity in ethnicity or culture is less balanced. Dutch men hold most senior positions. Within the hospital, this is somewhat understandable, as patients speak Dutch. However, in other programs this should be addressed more proactively. Diversity does not seem to be very high on the agenda. For example, it is not addressed in HR policy.

### 2.6.3. Talent management

Several areas, for example Neuroimaging, have many non-medical staff members who provide computational and technical support, essential to the research. The committee has the perception that it may be relatively easy to create tenured positions for medical staff (in combination with clinical work). But in modern hospitals it is becoming increasingly important to think about the need for non-medical staff members, for structuring data or for Artificial Intelligence. Non-medical academics are essential in this respect, and they require a career path.

People management is a challenge. It impacts the way that young talented staff is kept onboard. Because many scientists get a temporary contract, they must leave the university for six months after their contract. This is deleterious for retaining talent. Time and resources should be dedicated to work around this issue.

From the interview with mid-career scientists the committee learned that often transparency is lacking when it comes to positions and promotions. Some were suddenly promoted without knowing why and others did not know how to become eligible for promotion. The committee emphasizes the importance of clear and transparent promotion processes, to retain talented scientists.

The Young Amsterdam Neuroscience talent program is a good development. It offers clear benefits to participants in obtaining access to new training opportunities, resources, and connections. It also increases opportunities for collaboration. To further develop the functioning of this Young Amsterdam Neuroscience, the committee suggests the following actions:

- Better define the goal of the Young Amsterdam Neuroscience program and determine who can participate in this program. Currently, the program is mainly joined by young scientists from the hospitals, while it seems to lack visibility in the VU and UvA. Increasing visibility will lead to participation from across the institute;
- Young Amsterdam Neuroscience might profit

from a more bottom-up approach. The young and motivated scientists should be able to organize meetings amongst themselves to best fit their needs. These meetings should also include more specialized topics and reflections on what is needed for them as a group. By appointing a rotating chair, involvement and commitment will be stimulated while offering a great learning opportunity.

- The committee has the impression that talent management programs are research focused with plenty of opportunities for young scientists to learn how to set up their own group and become a PI or a professor. The committee wonders about other issues in talent development, such as clinical research skills, entrepreneurial skills or project management.

The committee suggests encouraging interaction not only at the PI level but – important - also at the PhD, postdoc and possibly the technician levels. In particular the postdoc group might benefit from increased interactions among their peers and from sharing of knowledge, ideally across Amsterdam Neuroscience programs. This should take place more often than once a year at the institute meeting.

## 2.7. Graduate School

The graduate school is well organized. The PhD candidates seem happy with the working atmosphere and culture. Most are well supported by supervisors and other people in their research departments and supervisors are very approachable. Most PhD candidates have weekly meetings with their main supervisor to discuss research progress and address any problems into which they might run. In addition, there are yearly meetings that focus on the PhD candidate's wellbeing and career perspectives. These evaluation moments include 360° feedback and offer them the opportunity to give feedback about the supervision. PhD candidates overall are very content with the supervision they get.

The success of a PhD program is, as it should be, measured by multiple parameters: duration of the

project (including time spend after contract ends), number of papers published, job opportunities afterward, and wellbeing of the students. Most PhD projects finish within the contract time, which is laudable. COVID-19 impacted many of the PhD projects, often resulting in a delay. All PhD candidates the committee talked to, informed that an extension of several months was offered to be able to finish their project.

Amsterdam Neuroscience keeps track of the where recently graduated PhD candidates enter the job market. Job perspectives are incredibly positive, with most PhD candidates finding a position within 3 months after defending their thesis.

The main recommendation by the committee is to also stimulate collaboration at the PhD candidate

level within the institute. Many PhD candidates are not aware of collaboration opportunities or cannot find the right people to collaborate with. Supervisors can be instrumental in this, but a clearer website showing the different research programs and various expertise could help. In addition, more activities could be organized for PhD candidates across different research programs. This stimulates to get to know each other across the institute and strengthens their network.

A possible threat for the PhD trajectory could be publication pressure. There is a strict requirement of two scientific first author papers. However, depending on the (sub)field in which the PhD candidate is working this might not always be a realistic goal.

## III. Assessment of SEP-criteria

### 3.1. Compulsivity, Impulsivity and Attention

CIA is an active program with high levels of commitment and participation of its members. There are numerous - well attended - brainstorm meetings, speed dating around seed funding opportunities, and elevator pitches presenting what people are working on. PhD candidates are not yet actively invited to participate in these activities, they could be invited to attend from the start to elaborate their network and mindset.

The atmosphere is quite informal, without a strict hierarchy, and with many contacts between program members. PI's have the responsibility to write junior research staff into grant proposals, thus enabling them to work on new projects. The care and science program could be integrated in the MD-PhD trajectory, e.g., during rotations, to create a research mindset. However, this should be considered carefully, considering the workload that such a combined program would present to young clinician-scientists.

#### 3.2.1. Research quality

The Compulsivity, Impulsivity and Attention (CIA) program is very strong. It includes several leaders in the field, both on the clinical and the preclinical side. In particular the research on brain stimulation and neuromodulation approaches is of outstanding quality. In this respect the program is really benefiting from strong translational approaches, with forward and reverse translation from animals to humans. The program clearly attributes its success to Amsterdam Neuroscience. The scientists involved are enthusiastic about the institute. This sentiment was voiced from the level of PhD candidates up to the 16 program leaders.

The CIA-program shows strong strategic developments in using multilevel biological assessments, especially EEG and neuroimaging to devise personalized treatment approaches. While this personalized treatment approach is one of the biggest challenges in psychiatry, the

approaches taken here, especially within the field of neuromodulatory interventions, are promising. This work will be supported by the planned expansions to molecular/genetic biomarkers. These are also highly translatable to animal models. Another big strength of the CIA program is its ability to perform lifespan research, from childhood towards adolescence and into adulthood. This approach is well supported by the inclusion of new PIs from child and adolescent psychiatry.

#### 3.2.2. Relevance to Society

CIA's research that is done is relevant to large groups of young people in Dutch society. The societal impact as shown in the heatmaps shows good scores on potential relevance to policy and clinical guidelines. Patients are well involved in the various research projects, invited to help writing proposals and sometimes co-authoring publications. *Scientists* attend meetings of patient groups, and they integrate patient needs in their research agenda. The fact that *the program has no* problems including enough patients in large trials is testimony to the quality of the program's engagement with target groups.

It turned out to be hard to find translational partners in industry. Nevertheless, it may be worthwhile to try and set up collaboration with industrial partners with the help of the Industry Alliance Office.

#### 3.2.3. Viability

This strong research group has a sharp vision and focus. After the merging of the departments at the Amsterdam UMC, the program will be well equipped to face future challenges.

Given the complementary strengths of the two psychiatry departments in brain stimulation and neuromodulation, a timely merger would be a tremendous benefit for the program, as well as for Amsterdam Neuroscience. A unified group would hold one of the strongest, unified neurostimulation units internationally. Being split in the two separate sites hampers progress. The committee is aware that this is work-in-progress.



As indicated by the program leaders, a future integration of child and adolescent with adult psychiatry would provide unique assets, given the enormous importance of understanding health and disease trajectories over these critical periods in life. It would help in establishing an even stronger transitional psychiatry program. Better access to infrastructural facilities would even further enhance the success of the program. It is not clear to what extent CIA will benefit from the

new core facilities in the new ADORE building.

#### *3.2.4. Recommendations*

The CIA research program eagerly awaits the upcoming merger of the two psychiatry departments. There is a strong bottom-up willingness to cooperate, but opportunities are left unused. There seems to be a perceived lack of leadership in moving forward with the merger of the two psychiatry departments.

## 3.2. Brain Imaging

### 3.2.1. Research quality

Some of the highlights of the Brain Imaging program, described in the self-evaluation report, include the development and clinical application of advanced brain imaging techniques focused on multi-modal imaging, precision medicine and minimally invasive brain imaging. This applies particularly to advanced imaging tools and techniques to advance drug-targeting strategies. Furthermore, the program focuses on translational neuroscience including small animal neuroimaging (micro-EEG/PET/SPECT/MRI) via institutional funding. With Big Data and AI emerging as critical methodologies for neuroscience, collaborations with physics and mathematics groups have been intensified via Proof of Concept and Amsterdam Neuroscience funding.

Performance measured as scientific output and grants is impressive. Compared to their size and budget, the neuroimaging group is extremely well performing within the Amsterdam Neuroscience. This is reflected in the number of peer-reviewed publications, the number of PhD graduations and the successful acquisition of external grants (VENI, VIDI, TOP, Abipat, ENBIT, ERC Consolidator etc.). Neuroimaging methodologies rarely publish in the top-level journals, but compared to other groups in the field, the scientific output of the Brain Imaging program is excellent.

All brain imaging facilities are currently relocated to the VUmc campus and encompass radiochemistry and PET, whereas SPECT traditionally has been done at AMC. These sites are also used for general imaging as well. This causes competition for imaging slots. Particularly, PET slots are in demand by other disciplines, oncology taking up quite some resources. The move of facilities within VUmc is almost completed, except for hot lab, but the expectation is that by the end of this year, the imaging center will be fully operational with all the main imaging VUmc modalities being in one building. Another neuroimaging facility is located at the Spinoza center, also including 7T MR. MR-facilities are

present on all sites; the institute of psychology also has its own MR-scanner.

Acquiring brain images is quite costly. Research scanning costs for research are paid from grants. One suggestion is to ask researchers for a (small) financial contribution for performing or assistance with data analysis as part of a neuroimaging pipeline. The committee understood that a transparent payment system is currently underway, to better standardize these prices across sites. Importantly, current charges do not include data analysis which can be quite heavy and often needs involvement of data analysis specialists.

### 3.2.2. Societal relevance

The program team has set up an Amsterdam Neuroscience Neuroimaging database and analysis pipeline. One of the PI's is a driving force behind several ENIGMA programs which involve sharing brain MR across international institutions. The program team has not yet considered adapting common data structures, such as OpenNeuro, although this offers a well-tested approach to standardizing brain images formats and storage.

The neuroimaging field increasingly needs to engage scientists from mathematics, data science, physics, i.e., scientists that are not MD's or hospital physicists. The committee proposes to negotiate joint appointment constructions, e.g., with 50% employment at the hospital, 50% at the math/data science faculty. To meet the increasing demands for AI and open science the committee proposes to establish a neuroimaging core facility to engage with data processing and analysis. This could also help to join the experts across the various Amsterdam sites. Such a core facility should include non-academic staff as well, to curate and quality control data, as well as store data in a standardized manner. The committee furthermore proposes the program to consider adapting standards, such as OpenNeuro.

### 3.2.3. Viability

The AI part of the program has been strengthened by the close collaboration with the department of

Biomedical Engineering and Physics. Four young scientists supported by grants from Amsterdam Neuroscience received tenure positions after their postgraduate careers took a fly after receiving a proof-of-concept (PoC) or regular grant from the institute.

#### *3.2.4. Recommendations*

The scattered location of the neuroimaging facilities across three different sites and the lack of a unified governance structure is seen as problematic by the committee and should be forwarded to the hospital management (Amsterdam Research Board).

### 3.3. Neurodegeneration

This is a highly successful program in terms of scientific output, grants obtained and relevance to society. The research topics of the Neurodegeneration program encompasses Alzheimer's disease (AD), Parkinson's disease, (PD), Frontotemporal dementia (FTD), and Dementia with Lewy bodies (DLB). The translational research and team science has been stimulated by various local (seminars, PoCs, TKI-PPP) and national initiatives, leading to novel collaborations between basic and clinical scientists and initiatives to integrate patient care and research.

ProPark is a large recently funded multicenter cohort research study of major importance for translational research. It identifies scientific problems in collaboration with industry. Amsterdam Neuroscience supports all stages. The program team makes widely use of core facilities (biobank, genetics, imaging) for their research, but also greatly capitalizes on their large patient cohorts.

#### 3.3.1. Research quality

The Alzheimer research group is large, both internationally and within Amsterdam Neuroscience, with high-end publications and an impressive amount of external funding. The program is internationally leading in its field. The change of leadership – seen as critical for the program - seems to have been smooth. The Parkinson research group has increased its scientific impact in the period of the review towards high-impact publications. The group is capitalizing on core facilities and its expertise in deep brain stimulation. It is now also establishing its own patient cohorts, which will be instrumental for future research.

Compared to the midterm review, the two groups now interact more and FTD has moved to the same campus as PD. The collaboration within the program has benefited from Amsterdam Neuroscience seeding grants. The program also stresses that the institute offers a wonderful opportunity for multi-center (cohort) studies, which are essential for translational studies.

One important strength of this program, which contributes to its success, is its focused strategy. There is a comprehensive vision and strategy directing the research. In addition, the group truly embraces the opportunities provided by Amsterdam Neuroscience as an institute for multi-center (cohort) studies.

Amsterdam Neuroscience is considered as instrumental for the development of the program; the institute supports infrastructure and core facilities, e.g., the biobank. As an example, the biobank enables detection of specific early biomarker for later development of Alzheimer's Disease. Amsterdam Neuroscience enables the translational aspects with the Alzheimer's Centre of Amsterdam UMC for neurodegenerative disorders. The Proof-of-Concept grants have stimulated cross-boundaries research and have been instrumental to bridge between the Alzheimer's and Parkinson's groups. The stimulation of cross-boundaries research more broadly benefits from the matrix structure, e.g., the neuroimaging facility and collaborations have been initiated through Amsterdam Neuroscience. Adore is seen as particularly important for the future research within the team.

#### 3.3.2. Relevance to Society

The Neurodegeneration research area is highly relevant to society, not in the least because of the changing demographics. The program organizes meetings for patients and their relatives. The clinical scientists engage with the AD patient groups although it is not clear whether patients (relatives) are asked for input to clinical trials or research as such. The interaction with patients (relatives) should ideally start at the inception of the project where stakeholders could have an input on, e.g., study design. At the end of project, it is important to disseminate the results and encourage patients/relatives to ask questions.

The program team confirms that they make federated research data publicly available, but because of GDPR issues, they cannot make genetic data available. There is some external data exchange approved via data protection

agency or similar boards. Although most grants today require inclusion of a section on data sharing, it is not always obvious how it is implemented in practice.

### *3.3.3. Viability*

The program team has a strong focus on talent management and sustainability. It recruits master's and pre-PhD students lets them "grow" within the program. The PhD candidates in the program are happy with the supervision provided and recognizes a good learning environment within Amsterdam Neuroscience.

### *3.3.4. Recommendations*

Apart from general recommendations that are

provided in Chapter 2 and apply for the entire Amsterdam Neuroscience, a few specific recommendations apply to the Neurodegeneration program. The committee recommends that the program team considers engagement of patients from the inception of research projects. It also recommends that the teams within Neurodegenerative disorders continue to collaborate and to act in synergy.

Since 90% of the AD research expenses is covered by external grants the committee recommends that internal funding is made available to secure the sustainability of the research group.

## 3.4. Complex Trait Genetics

### 3.4.1. Research quality

The work in complex trait genetics includes fundamental discoveries on human brain development and advanced genetic studies in major diseases. Despite being one of the smaller programs of Amsterdam Neuroscience, the research of the complex trait genetics program is outstanding and supported by some of the most prestigious grants (including local and international funds like ERC). It is home to very visible scientists that belong to the best genetics groups worldwide. In the program, important breakthroughs are produced that were published in journals that are among the most visible internationally. Attesting to its high quality and productivity, with a research budget that is smaller than many other programs, it produced many high impact publications. To the committee it is evident that these “top researchers” can (and will) serve as mentors for the younger colleagues in this program.

An important achievement of this program over the past years has been to connect genetics with neuroscience in Amsterdam. The previous round of seed funding was in part used for this purpose: it was deployed in a democratic fashion where the group of PIs jointly made funding decisions as to attract new disciplines and provide opportunity to younger colleagues. The complex trait genetics program is now in an excellent position to take on the next wave of challenges in its field. The support of the institute is going to be instrumental, but given the quality of the program, this will pay back in visibility and grant income for the entire institute.

### 3.4.2. Relevance to Society

Genetic discovery is an essential aspect of understanding disease processes and as such this is important for basic scientists and for industrial application as is evident from the program’s very well-cited patent applications. This (type of) work is visible, and the complex trait genetics program has appeared amply in media, well-above average.

### 3.4.3. Viability

There is an excellent science vision in this program, including initiatives that were taken and platforms that have been set up. In the program there is the understanding that biobanking and bioinformatics will be important in the future. Also, the importance of connecting the complex trait genetics scientists both within the group and across the institute is acknowledged as an important challenge. A clear plan and vision for these important aspects was, however, less clear to the committee.

Complex genetics as a discipline is facing challenges that this program will also need to tackle. However, it is in an excellent position to do so. The field is, in addition to gene and variant discovery, moving to functional studies, where the position of these variants and their multiple and complex interactions need to be interpreted in the context of disease. This will necessitate to expand towards additional methodology. In this respect, the embedding within Amsterdam Neuroscience can be an enormous asset. The leadership should plan out how it will leverage the capacity and knowledge on animal and human models of disease into the complex trait genetic labs.

The Neuroscience Amsterdam mission statement could serve as a guideline for a long-term vision of the Complex Trait Genetics program. An important part of such a plan involves bringing the scientists of this program together more frequently. It could also be considered to encourage this not only at the PI level but – importantly - also at the PhD, Postdoc and possibly the technician level.

In previous years the complex trait genetics program distributed seed funding, and this has successfully leveraged new methodology and ideas. A possibility is to repeat this process providing explicit opportunity to new and/or younger colleagues and to also include other programs of Amsterdam Neuroscience.

### 3.4.4. Recommendations

There is, and will be, an enormous need for

bioinformatics. This program is already strong on this aspect, but the knowledge is distributed somewhat fragmented. It could be considered to take a leading role in creating a structure, together with larger initiatives such as ADORE. By generating a knowledge base that provides local support, it might also benefit from central exchange of knowledge and new methodology, e.g., a central/decentralized system.

Biobanking will increasingly become a more critical aspect of complex trait genetics research, which requires coordination. Biobanking is decentralized and it will be helpful to develop a set of policies to streamline biobanking across Amsterdam Neuroscience. Given the importance of biobanking to this program the leadership of complex trait genetics could take an active role.

## 3.5. Neuroinfection and inflammation

### 3.5.1. Research quality

Amsterdam Neuroscience offers the opportunity to acquire unique cohorts. This research program exploits this opportunity well by initiating clinical trials. Both the multiple sclerosis (MS) and the infection components of this program are considered clear leaders in their respective fields. The Neuroinfection and inflammation (NII) program has a sizable number of publications, with 2021 being the best in the past years, including high citation indexes. In addition, the total research funding is way above average. This program has a nicely focused research strategy, and a clear translational mindset. COVID-19 severely impacted the inclusion of patients in trials, and this has not recovered yet.

There was highly active involvement and leadership in COVID19 research, including a big cohort study. This created massive opportunities, e.g., resulting in a biobank, which was used for both immunology and oncology research and broadened the view of the program. The activity created massive amounts of data, requiring a clear data structure which turned out to be very labor intensive. Clear regulations regarding data management from Amsterdam Neuroscience would be helpful. Although an MTA (material transfer agreement) is in place, legal procedures are often slow, taking an inordinate amount of time. On the other hand, the ethical approval from the ethics committee was fast.

A research nurse would be helpful to facilitate trial studies. However, to be really of added value, this nurse should have clinical experience with the disease(s). Finding such people is very hard, with a nationwide shortage of nursing staff.

The Industry Alliance Office is immensely helpful when it comes to start up trials. Their help saves a lot of work and supports pharma-trial preparations. For the future, more collaborations with biotech-companies are desired. However, despite multiple initiatives from this research program, the response/willingness from the companies is so far very limited and did not yet

result in a fruitful collaboration.

Time dedicated to research is yearly discussed with the head of the department. Although this differs across the years, the amount of time set for this seems realistic and sufficient.

### 3.5.2. Relevance to Society

Although program members are keen on data sharing, they struggle with sharing information from large cohort studies (open science) as privacy regulations impede such sharing. Setting up data sharing platforms, according to FAIR principles, seems nearly impossible. Researchers and clinicians feel hindered by unclear standards of data sorting, while again legal support is insufficient.

There is increasing involvement of patient organizations in determining research strategies and priorities. In addition, there is extensive scientific outreach, and the program members share information with patients. However, in general, this communication sometimes feels a bit one-directional, and an increase in data supported prove of impact on society could be desirable.

### 3.5.3. Viability

Based on the SWOT analysis, the program added some research directions and is planning to do more single cell sequencing experiments. These experiments require good core facilities. The program started collaborating with the genomic core facility but encountered issues in communicating with that core facility. As a result, the program also often uses facilities outside of Amsterdam Neuroscience. Better coordination and clear strategic choices regarding the use and set up of the core facilities could be beneficial for all research programs. Currently, services of core facilities are not much cheaper than commercial parties. The challenge is how to make the collaboration more attractive for internal use.

The atmosphere in the program is very good. Group members are open and collaborative. Weekly meetings are structurally organized, and PhD candidates have sufficient peers to connect with. There are sufficient people to offer each



other support where needed. It was nice to see that a number of the questions during the site visit were redirected to one of the PhD candidates, indeed indicating an open work culture.

Although the one-day annual meeting of Amsterdam Neuroscience is highly appreciated - it is inspirational to be in contact with other programs – the connection to other programs is not very strong. Most of the work is done in the program's own centers.

#### *3.5.4. Recommendations*

Data sharing policy and regulations are a problem for this program, but also a structural problem within Amsterdam Neuroscience. With more invested time and money, a more structured and organized platform could be set up. A clear institute driven policy and regulation is required and needed for the continuity of high level and fast research. Also, look into more possibilities to outsource data analysis. With the increasing workload, this might save time and could lead to more automated data analyses processes.

## 3.6. Systems and Network Neuroscience

### 3.6.1. Research quality

The Systems and Network Neuroscience (SNN) program resulted from a SWOT analysis at the beginning of 2019. Selected co-workers from the initial Neurotechnology and Brain Mechanism research lines were regrouped into this new research program to form a better-balanced program with a wider perspective on the higher dimensional levels of brain organization. Combining both advanced technologies in neuroscience and computational methods across multiple disciplines the group has published in high-ranking journals.

The SNN program has an extensive network, and the program leaders know where to find each other. Many collaborations are initiated and ongoing. For PhD candidates lacking this network it might be harder to find their way.

SNN receives most funding from intermediate public bodies and non-profit organizations. Obtaining sustainable funding is acknowledged as a challenge for the future, the scientists would like to see more opportunities to apply for personal grants. It is acknowledged by SNN that Amsterdam Neuroscience has been helpful in initiating collaborations with more translational aspects to obtain funding. The Proof of Concept (PoC) or seed money is highly valued as it not only initiates collaborations, but also allows young talented scientists to boost their careers. It is also used to invest in the acquisition of more substantial grants.

The members of the research program are located at various institutes and research groups across Amsterdam (AMC, VUmc, VU, UvA and NIN). All groups have their own facilities and infrastructure. Under the umbrella of Amsterdam Neuroscience, collaborations are started between PIs of different research groups. Collaborations outside of Amsterdam Neuroscience are also initiated (i.e., with the virtual AI institute of the VU).

### 3.6.2. Relevance to society

As a fundamental research program, SNN scientists feel pressure when it comes to the interaction with the Industry Alliance Office. Within the program, pressure is felt to commercialize or valorize as this would be an increasingly important measure of the quality of the research within Amsterdam Neuroscience. The general feeling is that the pressure to valorize hampers the advance of fundamental research. The committee is of the opinion that Amsterdam Neuroscience should include the bench-to-bed strategy, but not each program by itself. Therefore, the committee thinks that the SNN program will benefit from the recommendation at institute level to have all programs relate to the bench-to-bed strategy. After all, fundamental research plays an important role in the institute's strategy, even if valorization does not take place within this program.

### 3.6.3. Viability

As the SNN program has been established recently, it remains to be seen how well it can succeed to obtain sustainable funding. The groups participating in this program are still strongly related to their own institutes and departments and the scientists are still in initial stages of connecting to each other. The committee is confident that they will find their way with increased interaction and collaboration within the program as a result.

The program has the wish to extend the computational infrastructure and to have access and interaction with computational personnel from the other programs. Many programs are doing similar work but are scattered across the institute. SNN does not have a sharp vision on how to achieve this and refers to the institutes and groups of the scientists for solving these problems with regard to data storage or computing facilities.

### 3.6.4. Recommendations

As the program is scattered across Amsterdam at various locations, a situation that is not going to change in the near future, it would strengthen the program as a whole to provide and share more

information about how to reach and find each other. This is especially valid to the less senior scientists. A dedicated website and hybrid meetings would be a possibility.

## 3.7. Neurovascular Disorders

### 3.7.1. Research quality

The Neurovascular Disorders program, a joint effort of neurology, neurosurgery and rehabilitation groups, is very active both in the Netherlands and internationally. Its output in terms of papers per year consistently exceeds one hundred per year throughout the period 2016-2021. The number of papers with an impact factor >10 is increasing over the years, up to 20 in 2021, and mean normalized citation scores and journal impact scores clearly outdo the global average. Grants obtained vary between 1 and 5M Euro per year. These aspects all support the very good quality of the research.

In the past, the program has clearly benefited from close collaborations with other vascular groups in the Netherlands in the MR CLEAN and CONTRAST consortia, for which they are applauded (Amsterdam was one of the three original MR CLEAN founders). Clinical vascular research nowadays, by its very nature, involves large cohorts and scientists from the program play a prominent national and international role.

The program leaders mentioned the lack of a central data analysis / statistics facility. Such support is indeed crucial to the type of work they are doing, and it has wider relevance to other clinical and basis science groups in the Neuroscience Institute. Whether such a facility should be part of the Institute or be more centralized at the UMC or university level remains to be determined.

In its SWOT analysis the program leaders define four research interests: acute ischemic stroke including pre-hospital triage and rehabilitation, subarachnoid and intracerebral hemorrhage, cerebral venous thrombosis, and subdural hematoma. In the presentation of top five publications, only papers on ischemic stroke and cerebral venous thrombosis are mentioned, while in the aggregate figures presented for the program, these four different lines cannot be discerned. Also, during the site visit with the program management, the program's focus was

not clearly provided. Thus, the committee got the impression of a program that is supported by (very good) ischemic stroke research, while the other topics are much less visible.

### 3.7.2. Relevance to Society

The outcome of the research in terms of societal relevance is unequivocal: the results from the intra-arterial thrombectomy trials have revolutionized the current treatment of ischemic stroke, benefited many patients, and have helped cutting health care costs in terms of nursing home admissions. To what extent results from the other program research lines have yielded similar benefits remains unclear to the committee.

When asked how the program's scientists involve patients as primary stakeholders in the design of their trials, meetings with patient organizations were mentioned. This will strengthen (perceived and actual) relevance of these trials. Patient engagement should be done at a national or even international level, but given the extensive collaborations of the principal investigators, such input may be in place.

The committee could not find any mention of a strategy to disseminate insights obtained from the research to the wider society. A more active approach – using social media, engagement with lay and patient organizations – should be considered.

### 3.7.3. Viability

The current program leaders are young and very active. The level of funding is good and in the upcoming years there remains ample opportunity to obtain additional funding from major organizations like the Dutch Heart Foundation, ZonMW and European funds. Moreover, data acquisition is a direct consequence of patient care, so a solid basis for clinical research is guaranteed.

The major threat to viability may be concentration of high-quality research activities in this small group of scientists. If one of them leaves Amsterdam, continuity may become problematic. Given the fact that acute stroke care is an important clinical activity in Amsterdam UMC,

continuous monitoring of research potential in young clinicians and scientists should be considered.

The situation regarding the vitality of the neurosurgery (subarachnoid hemorrhage, subdural hematoma) and rehabilitation parts of the program cannot be judged by the committee because of a lack of information.

#### *3.7.4. Recommendations*

Consider focusing this program on ischemic stroke and cerebral venous thrombosis and either drop 'subarachnoid hemorrhage' and 'subdural

hematoma' as research themes or develop them into separate programs.

Given the strengths of other programs in Neuroscience Amsterdam, the program could consider more joint projects, for example pharmacogenomics of stroke treatment or novel imaging modalities to predict stroke and stroke treatment outcome.

The program should develop a communication strategy when it comes to outreach to lay organizations and the general public.

## 3.8. Cellular and Molecular Mechanisms

### 3.8.1. Research quality

This program is outstanding with several visible and excellent scientists. It is noteworthy that the output of this program does not depend on one or a few scientists. On average, cellular, and molecular mechanism scientists have published more papers than other Amsterdam Neuroscience programs and -more importantly - their work (and publications) have been exceptionally visible. Among the contributions are community tools such as SYNGO that is currently the worldwide standard for annotation of synaptic proteins. This work was published in *Neuron* and is one of the best cited papers in the journal. The work in this program also includes fundamental discoveries on the workings of the synapse and neurons, major diseases of the brain, and body brain interactions (e.g., obesity). Within the program scientists interact visibly well, there is a level of trust between the PI's and excellent facilities were established to support the research. The research is amply supported by some of the most competitive grants, both nationally and internationally, and the program has an impressive international network (e.g., formal interactions with the Broad institute). Finally, the Cellular and Molecular Mechanisms program values the interactions with the Industry Alliance Office (IAO) very well, resulting in substantial industrial funding and collaboration.

An issue is the effective dissemination of technical expertise and facilities. It may be helpful to use a web-interface for this, but other possibilities could be explored.

### 3.8.2. Relevance to Society

The work of the cellular and molecular mechanisms program encompasses major diseases, and their focus is to understand the mechanisms as well as find ways to cure these conditions.

Bridging basic science and clinical research is not trivial but this group does an excellent job. This is, for example, evidenced by its strong

collaborations with the IAO. The program is also coordinating numerous visible projects and it organizes 'patients-meet-researcher' days and fundraisers in association with patient organizations. This program furthermore is vocal in terms of science policy, is keen on collaboration and it has created several technology platforms, e.g., iPSC platforms and associated automation, organoids, screening platforms, proteomics, metabolomics, advanced cellular imaging etc.

### 3.8.3. Viability

There is a strong vision on where this program is going in the upcoming years, including how to further strengthen and improve the program. It will invest in neurodevelopmental conditions and in bringing the science from the bench towards the clinic. Furthermore, focus will be on computational modeling in the development of neurotechnology and molecular/ cellular technologies and building on the already excellent iPS technology knowledgebase.

The program is scattered at various locations in Amsterdam, which is an impediment for science exchange. However, the PIs are developing ideas as how to bridge this gap, which may be examples to other programs. The scientists also realize the importance of collaboration beyond their own program, within the medical faculties and within Amsterdam Neuroscience. Furthermore, the need for, as well as their own involvement, in setting up a well-organized biobank is on the agenda.

Issues regarding animal experimental work is a major threat that that might impact this program. The program is alleviating this in part by investing in other systems such as fish and iPSC, but it has also found opportunities in moving to a different location, attesting to the "can do" attitude of this program.

### 3.8.4. Recommendations

The committee recommends that the leadership of program takes an initiating, active role in creating opportunities for scientists to meet in informal ways (e.g., happy hour), but also by providing the incentive to the students, postdocs, and technicians to meet their colleagues across

the various locations of this program.

There is increased emphasis on iPSC models within cellular and molecular mechanisms, requiring adequate biobanking. This is currently organized in a decentralized manner. The

committee recommends that the leadership of cellular and molecular mechanisms takes an active role to create common policies, and share protocols and common practice, ideally in conjunction with other program leaders.

### 3.9. Mood, Anxiety, Psychosis, Stress & Sleep

#### 3.9.1. Research quality

This very strong group includes a number of leaders in the field of mood, anxiety and stress research. The program is well integrated in Amsterdam Neuroscience and has been taking the seed funding for Proof of Concept (PoC) studies, as well as other bigger grant submission as incentives to interact and exchange. The breadth of PI's, covering the range from basic animal research to clinical research is much appreciated by the program scientists the committee talked to, and attributed to the vision of Amsterdam Neuroscience.

The importance of the program and Amsterdam Neuroscience is also perceived at the PhD and Postdoc level. The program leverages large cohort studies (especially the NESDA study), innovative clinical trials as well as animal research. The recent inclusion of the themes of stress and sleep into the program has been a very positive development. It aligns with psychiatric research increasingly exploring transdiagnostic risk factors and symptom domains. Also, it allows for better aligned translational studies from animal models to human studies. This is best exemplified in the stress and adversity research line, with complementary animal models and human studies. Very innovative and relevant are the studies on transgenerational inheritance of risk, again with mirrored animal and human studies.

The strength of the program is exemplified by an over the years steadily rising number of peer reviewed publications (over 250 in 2021), citation scores that are among the highest in the institute, and impressive amounts of yearly grants.

Overall, the program seems very well integrated in Amsterdam Neuroscience, PhD candidates and postdocs appear to benefit from being integrated in the larger community and there are a number of trans-program collaborations, mainly with CIA, CMM but also ND. Especially the transdiagnostic relevance of stress will allow many interesting interactions, also with neurology and

collaboration in the dementia and multiple sclerosis field have been initiated.

The on-going efforts to harmonize the different on-going studies, also by including relevant questionnaires in when cohorts are recontacted is laudable.

#### 3.9.2. Relevance to Society

Overall, stress, sleep, mood and anxiety disorders are of great societal relevance, given that they are the most common psychiatric symptoms. It is important that Amsterdam Neuroscience has a strong program in this area, and this is achieved. Patient involvement in study design is implicated for some studies and patient representatives interact with scientists. Specific outreach of this program has not been discussed, but there are huge possibilities in offering educational and diagnostic content and even therapeutic interventions through online resources – especially also in the context of stress and sleep.

#### 3.9.3. Viability

The program can build on large established cohorts that are among the most recognized world-wide. In addition, new clinical trials complement the portfolio. As said above, the inclusion of transdiagnostic risk factors and phenotypes increases the connections and translational potential between animal models and human research. In the area of stress, the program has also been active to increase collaborations on the national as well as EU level with STRESS-NL and STRESS-EU.

While not perceived as a strong negative for the program, the delay of the merger of the two psychiatry departments has also delayed the establishment of a clinical center for Mood and Anxiety disorders. Such a center would definitely increase the strength of the program.

While the interim move of the animal facility is seen as a hassle, the scientists agree that in the end they are looking forward to having access to a top-notch animal facility. The program noted that the high level of bureaucracy for animal research is a strong burden on scientists. Here a stronger



advocacy of Amsterdam Neuroscience for the importance of animal research in psychiatric disorders could help in reducing this burden.

#### *3.9.4. Recommendations*

Overall, this is a strong program with an important strategic shift to include stress and sleep. Data harmonization across the MAPSS program is important, but a huge potential also lies in including stress, sleep, mood and anxiety as transdiagnostic risk factors and symptoms in the other clinical programs, as already initiated. While transgenerational research cohorts have been

initiated, it is less clear how much focus is on longitudinal research, especially covering childhood and adolescence as important developmental risk stages. A timely merger of the two Departments of Psychiatry will also benefit the program.

As stated above, strong advocacy by the Neuroscience Institute or the universities for animal research is to be recommended. This preclinical part of the program will suffer from increased political interference or bureaucratic obstacles.

## IV. Recommendations

When evaluating different programs, the committee provides recommendations specific to that program. In this chapter, the committee sums up the most important recommendations at institute level. The committee also identifies areas that the institute cannot address alone, but which require external involvement (from the Executive Boards of Amsterdam UMC, Vrije Universiteit Amsterdam and the University of Amsterdam).

Before listing the main recommendations, the committee stresses that many and positive aspects were identified during the site visit. The institute is to be complimented for the developments and improvements made over the past few years (since the previous review). The committee's main conclusion is that Amsterdam Neuroscience consists of many strong research programs that broadly recognize the benefit and added value of Amsterdam Neuroscience. Of the many good practices, the committee identified, it wants to highlight two: the first is the seed funding, much was achieved with relatively small amounts, such as stimulating young scientists, boosting new research lines and creating time and space to write large research applications. The committee hopes for and encourages a new round of seed funding. In the discussions with the different programs, this was seen as extremely positive by all, and the committee would strongly support a continuation of this initiative. The new board of directors could use this initiative for strategic impulses, by for example putting more emphasis on cross program collaborations or PoC that would lead to valorization initiatives for example. The second good practice is the good functioning of the business development office (IAO).

### *External recommendations*

Governance: Due to involvement of different organizations, the overhead structure lacks transparency. This leads to undesirable inequalities within programs and within the institute. Also, the committee sees opportunities for further and stronger interactions between the

various institutes in Amsterdam.

Funding: Many scientists are paid from soft funding (especially among non-clinicians), which makes their careers at Amsterdam Neuroscience uncertain. In part, this is unavoidable, but an overly skewed balance carries risks. Also, Amsterdam Neuroscience has a small budget of its own, which limits the institute's steering power.

Facilities: The committee stresses the importance for Amsterdam Neuroscience, but also for other institutes, of joint facilities and their availability to all scientists (e.g., biobanking, data storage, computational facilities). Keeping the facilities up-to-date and making good use of them requires non-academic staff, e.g., for computational and technical support. Furthermore, challenges around animal research apply to more institutes than Amsterdam Neuroscience and should be jointly dealt with. While the committee acknowledges that the leadership is aware of the issues related to animal research, stronger political statement by Amsterdam Neuroscience as an Institute underscoring the importance of animal research in brain science would be welcome. Here connecting with organizations such as Hersenstichting or Alzheimer NL and their large societal visibility could be leveraged.

Legal issues: Many scientists and programs struggle with legal support. They often experience insufficient cooperation and slow responses, causing opportunities to fail.

### *Recommendations to Amsterdam Neuroscience*

The committee is positive about bench-to-bed strategy of the institute. By visualizing the contributions of the various programs to this strategy, each program can indicate how (and at what stage) it contributes to the strategy.

The institute's leadership recognizes that communication within the institute can and must improve. The committee encourages actions that improve communication, including improving the website (and move it away from the Amsterdam UMC support) to offer a platform for information exchange about different expertise, technologies,

and instruments. Having this online would ensure that this information is easily accessible to scientists at all career levels, including technician and increase possibilities for collaborations.

A great initiative is Young Amsterdam Neuroscience, initiated by the previous director. The committee recommends that the institute develop Young Amsterdam Neuroscience further, putting initiative with assistant and associate professors, and making clear who can be part of it. It would also be good for postdocs and PhD candidates to have more networking opportunities within the programs and within the institute. The institute may make more use of its good name to make connections with national and international organizations, e.g., EBRAINS. Formalizing national and international collaborations can help in branding of Amsterdam Neuroscience as a major national and

international player.

Although the committee was missing information on the diversity within the different programs, it sees need to increase diversity. While hiring is done at the university level, an atmosphere of welcoming international members by holding all Amsterdam Neuroscience meetings in English would support inclusivity. Amsterdam Neuroscience should ensure that a view on inclusivity is visible and make clear it is instrumental for the success of the institute.

The committee stimulates Amsterdam Neuroscience to formulate a definition of societal relevance for the institute, to which the programs can relate. It includes valorization and translational research, but also includes interaction with society and patients rather than a knowledge push.

# Appendices

## Appendix 1: The SEP Criteria and Aspects

The committee was requested to assess the quality of research conducted by Amsterdam Neuroscience as well as to offer recommendations to improve the quality of research and the strategy of Amsterdam Neuroscience. The committee was requested to carry out the assessment according to the guidelines specified in the Strategy Evaluation Protocol. The evaluation included a backward-looking and a forward-looking component. Specifically, the committee was asked to judge the performance of the unit on the main assessment criteria and offer its written conclusions as well as recommendations based on considerations and arguments. The main assessment criteria are:

- 1) **Research Quality:** the quality of the unit's research over the past six-year period is assessed in its international, national or – where appropriate – regional context. The assessment committee does so by assessing a research unit in light of its own aims and strategy. Central in this assessment are the contributions to the body of scientific knowledge. The assessment committee reflects on the quality and scientific relevance of the research. Moreover, the academic reputation and leadership within the field is assessed. The committee's assessment is grounded in a narrative argument and supported by evidence of the scientific achievements of the unit in the context of the national or international research field, as appropriate to the specific claims made in the narrative.
- 2) **Societal Relevance:** the societal relevance of the unit's research in terms of impact, public engagement and uptake of the unit's research is assessed in economic, social, cultural, educational or any other terms that may be relevant. Societal impact may often take longer to become apparent. Societal impact that became evident in the past six years may therefore well be due to research done by the

unit long before. The assessment committee reflects on societal relevance by assessing a research unit's accomplishments in light of its own aims and strategy. The assessment committee also reflects, where applicable, on the teaching-research nexus. The assessment is grounded in a narrative argument that describes the key research findings and their implications, while it also includes evidence for the societal relevance in terms of impact and engagement of the research unit.

- 3) **Viability of the Unit:** the extent to which the research unit's goals for the coming six-year period remain scientifically and societally relevant is assessed. It is also assessed whether its aims and strategy as well as the foresight of its leadership and its overall management are optimal to attain these goals. Finally, it is assessed whether the plans and resources are adequate to implement this strategy. The assessment committee also reflects on the viability of the research unit in relation to the expected developments in the field and societal developments as well as on the wider institutional context of the research unit.

During the evaluation of these criteria, the assessment committee was asked to incorporate four specific aspects. These aspects were included, as they are becoming increasingly important in the current scientific context and help to shape the past as well as future quality of the research unit. These four aspects relate to how the unit organizes and performs its research, how it is composed in terms of leadership and personnel, and how the unit is being run on a daily basis. These aspects are as follows:

- 4) **Open Science:** availability of research output, reuse of data, involvement of societal stakeholders.
- 5) **PhD Policy and Training:** supervision and instruction of PhD candidates.
- 6) **Academic Culture:** openness, (social) safety and inclusivity; and research integrity.
- 7) **Human Resources Policy:** diversity and talent management.

## Appendix 2: Programme of the site visit

27 September 2022 – Crown Plaza Hotel		
18.00	Meet & Greet with Directors	
19.30	Committee Introduction Meeting	
28 September 2022 – ALMA conference rooms		
8.30	Meet & Greet & Welcome	
9.00	Kick-off and welcome with directors and management team of Amsterdam Neuroscience	
10.30	<i>Coffee break</i>	
10.45	<b>Round 1</b>	
	Compulsivity, Impulsivity and Attention	Brain Imaging
11.30	<i>break</i>	
11.45	<b>Round 2</b>	
	Neurodegeneration	Complex Trait Genetics
12.30	<i>Lunch break</i>	
13.00	Pecha kucha's of 9 selected PhD students	
14.00	Dialogue with PhD students	
14.30	<b>Round 3</b>	
	Neuroinfection and inflammation	Systems and Network Neuroscience
15.15	<i>break</i>	
15.30	<b>Round 4</b>	
	Neurovascular Disorders	Cellular and Molecular Mechanisms
16.15	<i>break</i>	
16.30	<b>Round 5</b>	
	Mood, Anxiety, Psychosis, Stress & Sleep	Young Amsterdam Neuroscience
17.15	Wrap up day 1 – committee session	

29 September 2022 – ALMA conference rooms		
8.30	Consensus meeting part 1 (and writing session)	
10.30	Feedback dialogue with new team of directors	
11.00	Consensus meeting part 2 (and writing session)	
13.30	Closure with oral presentation by chair	
14.15	End of site visit	

## Appendix 3: Quantitative data

Table 1: Research staff in FTE

<i>All personnel</i>		Affiliations subtotals								
Year	Total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
2016	863	89	48	201	50	137	119	40	100	96
2017	1025	114	62	261	80	182	149	64	128	114
2018	877	118	51	244	83	177	137	74	132	109
2019	888	122	61	252	73	190	147	84	145	98
2020	877	111	58	225	73	179	142	76	120	90
2021	784	95	61	216	78	150	106	71	102	88

<i>PhD candidates</i>		Affiliations subtotals								
Year	Total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
2016	416	43	23	97	24	66	57	19	48	46
2017	479	53	25	117	37	85	70	30	60	53
2018	439	40	18	108	32	82	67	32	54	39
2019	453	58	20	145	33	81	86	50	84	44
2020	427	55	19	137	32	70	72	37	70	35
2021	376	47	23	128	31	60	52	36	54	35

Table 2: Main categories in research output 2016-2021

2016	Total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed article	1242	123	52	221	91	194	149	123	105	184
Non-Refereed article	15	2	1	2	2	3	0	0	2	3
Books	1	0	1	0	0	0	0	0	0	0
Book chapters	10	0	0	6	0	2	0	0	0	2
PhD theses	105	10	6	42	5	14	7	5	13	3
Conference papers	8	3	0	0	0	0	0	1	2	2
Professional publication	35	1	4	4	0	13	2	2	2	7
Publications aimed at general public	5	0	0	1	0	0	2	0	1	1
Other research output	13	0	0	1	0	0	2	1	4	5
Total publications	1434	139	64	277	98	226	162	132	129	207
With impact $\geq 10$	<b>Subtotal</b>	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	143	4	7	25	29	22	16	6	5	29
With impact $\geq 5 < 10$	<b>Subtotal</b>	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	313	27	16	53	21	60	35	33	14	54

2017	Total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed article	1264	123	19	295	99	161	191	96	76	204
Non-Refereed article	4	0	0	0	0	1	0	0	1	2
Books	2	0	0	0	0	2	0	0	0	0
Book chapters	15	3	0	2	1	1	0	3	0	5
PhD theses	60	11	1	17	2	5	5	5	9	5
Conference papers	3	3	0	0	0	0	0	0	0	0
Professional publication	27	1	0	2	1	3	5	1	6	8
Publications aimed at the general public	4	0	0	0	0	0	0	0	2	2
Other research output	30	1	0	2	3	3	6	9	4	2
Total publications	1409	142	20	318	106	176	207	114	98	228
With impact $\geq 10$	<b>Subtotal</b>	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	130	2	3	27	26	17	16	10	9	20
With impact $\geq 5 < 10$	<b>Subtotal</b>	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	316	20	6	90	17	46	61	24	9	43

2018	Total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed article	1239	121	46	235	67	191	158	99	95	227
Non-Refereed article	25	2	2	0	2	4	4	6	4	1
Books	1	0	1	0	0	0	0	0	0	0
Book chapters	6	0	0	2	0	0	0	0	0	4
PhD theses	99	10	6	41	4	11	6	5	13	3
Conference papers	8	3	0	0	0	0	0	1	2	2
Professional publication	24	1	0	2	0	2	3	3	8	5
Publications aimed at the general public	1	0	0	1	0	0	0	0	0	0
Other research output	4	0	0	1	0	0	2	1	0	0
Total publications	1407	137	55	282	73	208	173	115	122	242
With impact $\geq 10$	<b>Subtotal</b>	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	160	2	2	30	23	28	21	12	13	29
With impact $\geq 5 < 10$	<b>Subtotal</b>	bi	nt	bm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	284	19	4	64	10	65	49	33	10	30



2019	Total	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed article	1338	157	33	205	92	234	190	127	101	199
Non-Refereed article	50	3	0	9	2	9	10	5	6	6
Books	0	0	0	0	0	0	0	0	0	0
Book chapters	23	4	0	10	3	2	0	1	1	2
PhD theses	83	8	7	9	4	15	18	6	6	10
Conference papers	13	7	0	0	0	3	0	1	2	0
Professional publication	71	1	2	4	1	15	7	4	17	20
Publications aimed at general public	2	0	0	0	0	1	0	0	0	1
Other research output	11	1	1	1	0	5	1	0	1	1
Total publications	1591	181	43	238	102	284	226	144	134	239
With impact $\geq 10$	<b>Subtotal</b>	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	175	7	6	32	27	41	20	7	15	20
With impact $\geq 5 < 10$	<b>Subtotal</b>	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	317	27	10	61	24	53	62	25	21	34

2020	Total	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed article	1315	125	31	207	86	238	184	119	95	230
Non-Refereed article	61	5	2	10	6	9	5	7	7	10
Books	0	0	0	0	0	0	0	0	0	0
Book chapters	15	1	2	1	0	3	2	2	2	2
PhD theses	86	8	4	14	7	14	19	8	4	8
Conference papers	9	7	0	0	0	1	0	1	0	0
Professional publication	64	3	1	5	2	10	3	5	15	20
Publications aimed at the general public	0	0	0	0	0	0	0	0	0	0
Other research output	24	6	0	2	0	3	1	1	3	8
Total publications	1574	155	40	239	101	278	214	143	126	278
With impact $\geq 10$	<b>Subtotal</b>	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	175	7	2	33	34	32	15	14	10	28
With impact $\geq 5 < 10$	<b>Subtotal</b>	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	354	33	4	61	14	63	72	38	11	58

2021	Total	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed article	1597	187	41	203	105	258	229	176	132	266
Non-Refereed article	74	7	2	11	9	15	13	7	6	4
Books	2	0	0	0	0	0	0	0	1	1
Book chapters	17	4	0	9	0	1	0	1	1	1
PhD theses	90	5	1	23	1	16	9	12	6	17
Conference papers	26	25	1	0	0	0	0	0	0	0
Professional publication	40	0	0	3	1	5	3	2	10	16
Publications aimed at the general public	3	0	1	0	0	0	0	1	0	1
Other research output	48	9	11	3	3	2	8	3	3	6
Total publications	1897	237	57	252	119	297	262	202	159	312
With impact $\geq 10$	<b>Subtotal</b>	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	276	16	17	34	32	70	41	20	12	34
With impact $\geq 5 < 10$	<b>Subtotal</b>	bi	snn	cmm	ctg	nd	nii	ndis	cia	map
Refereed articles (selected output)	256	42	4	42	17	39	47	10	13	42

Table 3: funding in FTE

2016	Grand total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
		k€	k€	k€	k€	k€	k€	k€	k€	k€
<b>Total</b>	<b>€ 41.978.650</b>	1.878	1.024	9.989	2.855	9.118	4.537	1.234	4.571	6.773
1st flow	€1.450.000	100	50	480	320	200	150	50	50	50
2nd flow	€26.347.126	545	547	8.237	2.331	2.432	1.666	1.184	4.421	4.984
3rd flow	€4.041.767	350	-	511	204	1.766	1.161	-	-	50
4th flow	€10.139.757	883	427	761	-	4.720	1.560	-	100	1.689

2017	Grand total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
		k€	k€	k€	k€	k€	k€	k€	k€	k€
<b>Total</b>	<b>€49.405.912</b>	2.222	2.268	13.911	3.002	11.926	5.565	5.241	1.622	3.649
1st flow	€3.546.691	520.493	249	546	56	73	738	941	133	292
2nd flow	€27.725.790	1.534	2.000	6.412	2.433	6.119	1.798	2.947	1.489	2.993
3rd flow	€10.514.423	-	-	3.475	514	3.877	1.162	1.338	-	149
4th flow	€7.619.008	167	19	3.478	-	1.857	1.868	15	-	215

2018	Grand total	bi	nt	bm	ctg	nd	nii	ndis	cia	map
		k€	k€	k€	k€	k€	k€	k€	k€	k€
<b>Total</b>	<b>€46.898.432</b>	4.363	2.789	9.843	1.779	14.404	3.570	3.412	2.746	3.992
1st flow	€2.080.235	559	50	606	-	-	145	649	-	71
2nd flow	€23.627.387	2.919	2.489	4.404	909	6.415	498	636	1.597	3.761
3rd flow	€11.118.757	88	250	3.635	870	2.059	914	1.993	1.150	160
4th flow	€10.072.053	797	-	1.198	-	5.930	2.014	133	-	-

2019	Grand total	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
		k€	k€	k€	k€	k€	k€	k€	k€	k€
<b>Total</b>	<b>€76.429.394</b>	9.152	5.123	10.135	6.909	16.026	16.823	2.834	4.130	5.299
1st flow	€2.475.000	275	275	275	275	275	275	275	275	275
2nd flow	€ 33.050.876	1.954	4.553	6.105	6.047	2.615	4.953	1.116	3.256	2.453
3rd flow	€ 20.617.131	6078	236	1.814	355	8.947	5.778	522	584	1.773
4th flow	€ 20.286.387	6.315	59	1.941	231	4.189	5.817	921	15	797

2020	Grand total	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
		k€	k€	k€	k€	k€	k€	k€	k€	k€
<b>Total</b>	<b>€ 55.337.353</b>	4.610	1.614	5.894	3.843	18.151	8.882	3.118	1.855	7.439
1st flow	-	-	-	-	-	-	-	-	-	-
2nd flow	€ 18.449.232	343	447	1.696	1.288	6.431	2.606	259	637	4.743
3rd flow	€ 23.774.947	3.688	855	3.679	2.213	5.021	3.378	1.621	624	2.697
4th flow	€ 13.113.174	579	313	519	342	6.699	2.828	1.239	594	-

2021	Grand total	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
		k€	k€	k€	k€	k€	k€	k€	k€	k€
<b>Total</b>	<b>€ 75.838.309</b>	3.169	7.582	11.789	2.566	22.442	9.828	1.596	13.128	3.738
1st flow	€ 415.921	-	-	366	-	-	25	-	-	25
2nd flow	€ 32.088.842	1.238	855	3.745	1.939	5.637	5.964	406	8.676	3.628
3rd flow	€ 29.435.643	746	6.691	2.845	528	10.829	3.088	1.164	3.531	14
4th flow	€ 13.897.903	1.185	36	4.833	99	5.977	751	25	921	71