# **Assessment of Research Quality**

# Neuroscience Campus Amsterdam 2009-2014

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# 1. Introduction

# 1.1 Background

This report describes the assessment of research conducted at the Neuroscience Campus Amsterdam (NCA) in the period 2009-2014. NCA is a research institute at the VU University Medical Center (VUmc) and VU University (VU) in Amsterdam, the Netherlands. The assessment was performed by an external assessment committee using the Standard Evaluation Protocol (SEP) 2015-2021. The primary aim of SEP assessments is to evaluate the quality and societal relevance of research and to provide advice to improve these where necessary. SEP assessments focus on the strategic choices and future prospects of research groups.

Target groups that are served by this assessment include:

- NCA's researchers and group leaders: they need to know how the quality of NCA research, its
  societal relevance, and its strategy are perceived by independent experts and how these
  elements can be improved;
- Board of deans of VU and VUmc: they wish to track the impact of their research policy;
- Dutch government: they want to know the outcomes of assessments in connection with the
  institution's accountability for expenditure and its own efforts to support an outstanding
  research system;
- Society and the private sector: they seek to solve a variety of problems using the knowledge that NCA research delivers.

# 1.2 Members of the assessment committee

The board of deans of VU and VUmc has appointed as members of the assessment committee:

- Professor Paul Matthews, chair (Imperial College London),
- · Professor Jonathan Flint (University of California, Los Angeles),
- Professor Jean Marc Fritschy (University of Zurich),
- Professor Catherine Lubetzki (Pierre and Marie Curie University),
- Professor Andreas Meyer-Lindenberg (Central Insitute of Mental Health, Mannheim; University of Heidelberg),
- Professor Trevor Smart (University College London),
- Professor Reisa Sperling (Harvard Medical School).

Professor Lubetzki could not attend the site visit due to personal circumstances, so she withdrew from the assessment committee. Dr Linda van den Berg (Washoe Life Science Communications) served as the secretary to the assessment committee. Short CVs of the committee members are provided in Appendix 1.

<sup>&</sup>lt;sup>1</sup> The SEP was drawn up and adopted by the Association of Universities in the Netherlands (VSNU), the Netherlands Organisation for Scientific Research (NWO), and the Royal Netherlands Academy of Arts and Sciences (KNAW). All research conducted at Dutch universities, university medical centres, and NWO or KNAW institutes is assessed once every six years in accordance with the SEP.

# 1.3 Procedures followed

The assessment committee evaluated NCA research based on NCA's self-assessment, its annual reports, and interviews with NCA representatives that were conducted during a site visit in November 2015. The site visit programme is provided in Appendix 2. The committee took into account international trends and developments in science and society as it formed its judgement. In addition, the committee bore in mind NCA's strategy while assessing the quality and relevance of the research.

# Qualitative and quantitative assessment of NCA research

The assessment committee based its judgement on three assessment criteria:

- 1. *research quality*, i.e., contribution to scientific knowledge, scale of research results (scientific publications, instruments, and infrastructure produced and other contributions to science);
- 2. relevance to society, i.e., quality, scale, and relevance of contributions (advisory reports for policy, contributions to public debates, etc.) targeting groups that NCA has itself designated as target groups (patients, the general public, students, and industry);
- 3. *viability*, i.e., the strategy that NCA intends to pursue in the future and the extent to which it can meet its targets in research and society during this period, the governance and leadership skills of NCA's management.

The qualitative assessments were supplemented by numerical scores (1–4) for each of the criteria.

# Assessment of NCA's PhD programme

The assessment committee also considered the supervision and instruction of PhD candidates at NCA. The assessment committee interviewed six PhD students during the site visit. The committee assumed that these individuals provided opinions that are representative of the group at large. In a separate session, the committee interviewed the PhD committee. The following topics were considered:

- institutional context of the PhD programme,
- · selection and admission procedure,
- quality assurance,
- programme content and structure,
- supervision and the effectiveness of supervision plans,
- duration, success rate, and exit numbers,
- career prospects and guidance of PhD candidates to the job market.

### Assessment of the NCA research integrity policy

The committee also considered NCA's policy on research integrity and the way in which violations of such integrity are prevented. This was discussed during the site visit. The committee was interested in how NCA deals with research data (i.e., data stewardship) and the extent to which a critical pursuit of science occurs at NCA.

# 1.4 Research unit under assessment: Neuroscience Campus Amsterdam

NCA is a research institute at the VUmc and VU. Built upon a rich but scattered neuroscience history, NCA was **founded in 2008** to create a research network organisation where scientists, students, and medical professionals collaborate in the field of **translational neuroscience**. NCA currently is the largest neuroscience research community gathered on one campus in the Netherlands. In 2014, NCA employed 451 researchers (181 PhD students, 144 post-docs, and 126 senior staff members, see Appendix 3 - Table 1 for further details).

NCA is a virtual organisation on top of traditional departments within several VU and VUmc faculties. It functions as a network organisation. Patient centres such as the Alzheimer Centre, the MS Centre, the Movement Disorder Clinic, the Centre for Childhood White Matter Disorders, and the GGZ inGeest clinic for Anxiety and Depression are major hubs in the NCA network. NCA's employees are appointed in VU or VUmc departments and they perform their research within NCA. Details about NCA's financing are provided in Appendix 3 (Tables 2 and 3).

All NCA research activities are interdisciplinary, i.e., clinicians and clinical researchers are working side by side with neuroscientists, geneticists, psychologists, epidemiologists, biophysicists, and statisticians. NCA's strongholds and international reputation rely on its work in understanding the human brain, clinical studies of its major diseases, development of advanced technologies, and a long tradition of behavioural genetics. Research at NCA is organised into **five research programmes** that collaborate intensively:

- 1. Brain imaging technology,
- 2. Brain mechanisms in health and disease,
- 3. Neurodegeneration,
- 4. Neuroinflammation,
- 5. Neurobiology of mental health.

# 2. Qualitative and quantitative assessment of NCA research

# 2.1 NCA's strategy and targets

NCA's **mission** is to study the brain and its diseases through an integrative approach, i.e., from molecule to bedside. NCA is **translational** and explicitly links basic science and clinical science. There is a strong focus on molecular neurobiology, including biophysics, genomics, systems biology of the synapse, and the genetic basis of brain function. NCA aims to advance neuroscience through innovative research and technology. In addition, NCA tries to find solutions that will benefit society through medicine and engineering. NCA's graduate programme offers training for national and international brain researchers in an environment of scientific excellence.

NCA was launched in 2008 to resolve disciplinary boundaries and to promote campus-wide collaborations. Hence, NCA has invested in building bridges by applying two strategies: 1) concerted funding of research support facilities and investments in advanced technology programmes and 2) financial support for novel initiatives to explore common research interests with campus-wide impact. In addition, valorisation, technology transfer, fund-raising, and European collaboration were used as instruments to strengthen NCA's core business.

NCA started off with ten research programmes. In 2011-2012, NCA research was reorganised into five research programmes to achieve greater focus. Each of these research programmes is coordinated by two programme leaders, often one with a clinical background and one with a more preclinical background.

NCA has set up an Industry Alliance Office (IAO) to facilitate public-private partnerships, i.e. commercially driven joint projects in the fields of target discovery, target validation, and biomarker research. The IAO is a dedicated front-office that offers NCA's scientific expertise, knowledge, and network to external commercial partners. Through the IAO, NCA organises guidance in clinical trials, collaborative programs with industry, and other research services to external stakeholders. The internal value of the IAO is to structure approaches to attract funding to support scientific research.

# 2.2 Assessment Neuroscience Campus Amsterdam as a whole

# Research quality

The committee rates NCA's overall research quality as **excellent**. NCA performs research of international quality across several areas of neuroscience. It also hosts many deeply phenotyped cohorts that promise a continuing contribution to the scientific mission. The institute has published an impressive number of articles in top scientific journals: 15-20% of NCA's peer reviewed papers were published in journals with an average impact factor of at least 9 in the period 2009-2014. In addition, several NCA investigators have been awarded prestigious grants, including the national Spinoza Prize and ERC grants.

# Relevance to society

NCA's research is **highly relevant** to society, in particular for the following societal groups:

- Patients: NCA research addresses severely debilitating neurodegenerative diseases and mental
  disorders. Its translational nature provides a strategy to best ensure that results are relevant to
  patients. The Industry Alliance Office contributes to bringing new discoveries to the bedside.
- **General public:** NCA's focus on prevention and early detection of brain diseases makes its research highly relevant to the general public. In addition, NCA engages in sharing its knowledge with the general public through outreach activities. Both the Alzheimer Center and the MS Center have extensive outreach programmes and several NCA staff members are involved in public outreach through the 'De Jonge Akademie' of the Royal Academy of Sciences.
- Students: NCA offers an excellent PhD training programme (see Chapter 3).
- Industry: The Industry Alliance Office (IAO) offers NCA's scientific expertise, knowledge, and network to external commercial partners. The committee thinks the IAO adds exceptional value to the university.

# Viability

Overall, NCA has many assets and the committee rates its viability as **very good**. The committee praised the **outstanding leadership** of NCA, especially noting the dynamic work attitude of the Director Arjen Brussaard who was seen as a key driver for collaboration across the NCA. The committee praised the extraordinary vertical integration of NCA research, i.e., the integration of basic science with clinical research, which is very successful. In addition, the committee praised NCA's collaborative spirit, both internally (i.e., between the five research programmes) and externally (i.e., in international research consortia).

The committee was impressed by the young ages and by the equal gender distribution of NCA staff. NCA offers a strong platform to support researchers for interaction and sharing of infrastructure in ways that extend their scientific capabilities. There is a collaborative spirit, which is promoted by the geographical proximity and the theme-based coordination of the research groups. The cohesive culture and the diversity in age and gender are very important to NCA's viability. In addition, the institute benefits from its integration with clinical care in hosting several world-class cohorts.

However, the committee also identified potential threats to the long-term sustainability of NCA, with the most important being:

- NCA's ability to recruit and retain the most talented researchers seems limited;
- Although NCA's team spirit is admirable, the institute structure seems slightly monolithic;
- Funding to support or develop important, larger elements of NCA's research infrastructure seems uncertain.

The committee will provide recommendations on how to deal with these concerns in Chapter 4.

# 2.3 Assessment Brain imaging technology programme

# Research quality

The committee rates the research quality of this programme in the period 2009-2014 as **very good**. While some parts of this programme are world class, others have fallen behind the very high standards they themselves set for these areas 3-4 years ago. In particular, multimodal imaging approaches, optogenetics, computational neuroscience, molecular imaging, and animal imaging were noted as potential areas for further expertise development.

### Relevance to society

The programme is **highly relevant** to society because its approach is truly translational. For instance, the group is developing minimally invasive programmes suitable for personalised medicine and drug targeting strategies. Early imaging markers of Alzheimer's disease and multiple sclerosis that can be utilized in prevention trials are also highly relevant.

# Viability

Overall, the committee rates the viability of this programme as **very good**. The programme has some great resources derived particularly from its close clinical links, but there are some concerns, with the most important being staff renewal. Recently, one key staff member left NCA and another senior staff member became part-time. NCA's management team acknowledges that this needs attention. In addition, the programme may need to consider new recruitment or partnerships to bring in additional expertise in areas potentially complementary with existing efforts that currently are under-represented, such as computational neuroscience and multi-modality molecular neuroimaging.

# 2.4 Assessment Brain mechanisms in health & disease programme

# Research quality

The quality of NCA's research on brain mechanisms in health & disease is **excellent**. The programme has an outstanding publication record and its work has international impact. For instance, the research on white matter disorders is recognised as seminal and is responsible for contributing several fundamental new insights into the classification and aetiologies of this group of diseases. Other research groups within this programme provide cutting edge technology or contribute to research infrastructure, in some cases providing key support to international efforts (e.g., the Genetics Cluster Computer of the Complex Trait Genetics group provides storage and nodes for the Psychiatric Genomics Consortium).

# Relevance to society

The work of this programme is **highly relevant** to patients. To provide an example, the Center for Childhood White Matter Disorders has made crucial contributions to the genetic diagnosis of patients with white matter disorders worldwide. In thirty years, the percentage of patients with white matter disease who have a DNA-confirmed diagnosis has increased from 60% to 90%.

# Viability

This programme's viability is rated as **excellent**. The research leaders are young and the programme is very focused. The programme has good connections with industry. The committee had the impression that some advanced research techniques may be somewhat confined to use in this group, so the committee encourages the researchers to share their techniques with the other NCA programmes where they might offer benefits.

# 2.5 Assessment Neurodegeneration programme

# Research quality

The committee rates the research quality of the Neurodegeneration programme as **excellent**. Research in this programme is conventional in approach, but is nonetheless very strong internationally. The programme hosts exceptional patient cohorts and large biobanks (e.g., Amsterdam Dementia cohort and Netherlands Parkinson cohort). In addition, the researchers study general population cohorts (e.g., Netherlands Twin Register and the impressive, unique 100+ study). There is good use of animal models and there are clear plans for developing new and useful lines. The committee praised the innovation of the genetic study of cognitively healthy ageing in the 100+ study and the strong research focus on proteomics of the synapse, linking basic and clinical science.

# Relevance to society

The Neurodegeneration programme is **highly relevant** to society because it addresses major public health problems such as Alzheimer's disease and Parkinson's disease. The researchers aim at understanding the mechanisms of neurodegeneration and preventing disease progression through early recognition. The basic science in this programme serves to develop diagnostic and prognostic biomarkers as well as new early treatments. The programme has an infrastructure for clinical trials. The patient cohorts have active public outreach programmes.

# Viability

The viability of this research programme is considered **excellent**, especially because of the strong cohort resources. The committee expects that the researchers will be able to capitalize on their large data sets. The programme has convincingly demonstrated its ability to attract external funding in a sustained way (see Appendix 3, Table 2) and it attracts fruitful collaborations.

# 2.6 Assessment Neuroinflammation programme

### Research quality

The Neuroinflammation programme is rated as **very good**. The basic science in this programme is good and the scientists have access to unique resources, e.g., large patient cohorts, post-mortem tissue, and research tools. Approximately 50% of all Dutch multiple sclerosis (MS) patients visit the VUmc MS center at least once. However, the committee believes that the programme currently risks having too little critical mass in strategically key areas to maintain its historically world-class efforts.

# Relevance to society

This programme is **relevant** to society as it contributes to the insight into the aetiology of a severely debilitating disease (MS). The researchers are working on methods to restore deficiencies in the

blood-brain barrier in patients and they are involved in clinical trials, though clinical evaluation needs further development. In addition, the neuroimaging work has led in the development of current criteria for the diagnosis of multiple sclerosis used internationally. However, the committee thinks that the broader relevance of the focus on astrocytes presented to the committee needs to be made more explicit, e.g., through links to other disease processes and the definition of clear pathways to impact.

# Viability

The viability of this programme is rated as **very good**. The programme has potential for excellence, but may be limited by the loss of one of its major leaders, who has not been replaced over the last six year period. The assessment committee believes that there is a strong case for integration of greater immunology expertise into the programme. The committee also believes that the researchers could enhance their connections with the other NCA programmes and other departments even further.

# 2.7 Assessment Neurobiology of mental health programme

# Research quality

The committee considers this programme **excellent.** NCA's mental health research is outstanding: the programme has an impressive publication list, innovative ideas, valuable cohorts, and excellent tools. It hosts top scientists. The researchers study innovative phenotypes, e.g., the exploration of the genetic basis of happiness in the Netherlands Twin Register. They have successfully engaged in large international collaborations such as the ENIGMA neuroimaging genetics study. Their studies have considerable impact in the field of psychiatry, e.g., they have revealed a distinction between melancholic and immuno-metabolic subtypes of depression and clarified neurostructural bases of affective disorders.

# Relevance to society

This programme is **highly relevant** to society because mental health disorders pose enormous personal, family and economic burdens by causing mental disability, and by their often chronic course. The programme has contributed significantly to our understanding of the mechanisms mediating vulnerability to mental diseases. For instance, NCA studies have added to the body of knowledge about adolescence as a vulnerable period for nicotine exposure. The programme is also studying interventions, e.g., the MOTAR study on the effect of combined treatment with anti-depressants and running therapy in patients with anxiety or depression. The cohorts have active public outreach programmes, including newsletters and annual patient days.

# Viability

The mental health programme at NCA is **strong.** Clinicians and researchers work together seamlessly in this programme. There is a good foundation for clinical research and there are excellent resources, e.g., the patient cohorts such as NESDA and a general population cohort (Netherlands Twin Register) with extensive phenotyping available.

# 2.8 Summary in numerical scores

The four possible categories are excellent (=1), very good (=2), good (=3), and unsatisfactory (=4). See Appendix 4 for an explanation of these scores.

	Research quality	Relevance to society	Viability
NCA as a whole	1	1	2
Brain imaging technology programme	2	1	2
Brain mechanisms in health & disease programme	1	1	1
Neurodegeneration programme	1	1	1
Neuroinflammation programme	2	2	2
Neurobiology of mental health programme	1	1	1

# 3. Qualitative assessment of PhD programme and research integrity policy

# 3.1 Quality and organisation of NCA's PhD programme

Overall, the committee was impressed by NCA's **very strong** PhD training programme. The programme is well structured and well financed.

# Institutional context of the PhD programme

NCA clearly considers graduate training a very important task. At the start of 2015, NCA hosted ~180 PhD students. The committee learned that NCA has a PhD committee, which is chaired by the director of NCA and has four members: the director of the Graduate School Neurosciences Amsterdam-Rotterdam (ONWAR) and representatives of the VUmc Alzheimer Center, the VUmc MS Center, and GGZ inGeest.

# Selection and admission procedure

The recruitment procedure for PhD students usually proceeds via a normal open call. Selection is performed by three to four NCA members. Candidates are chosen because of their motivation, knowledge, experience, and enthusiasm. The committee inferred that the selection procedure must be working well because the early drop-out percentage is very low (~6%).

# Quality assurance

The committee learned that NCA has implemented campus-wide PhD regulations. These regulations demand, in part, that at the start of each project the PhD students:

- receive instructions on the standard operating procedures for their studies, as outlined in a quality checklist;
- receive an NCA-specific protocol of instructions and list of courses to be followed;
- file a mandatory training and supervision plan for their PhD, which will be monitored by the supervisors.

# *Programme content and structure*

NCA has a 30 ECTS points training plan, which is partly incorporated into the Graduate School Neurosciences Amsterdam Rotterdam (ONWAR). Each PhD student selects courses based on a personal profile. Students are encouraged to select courses that broaden their horizons. On average, roughly half of the training plan is completed at ONWAR, with the remainder followed elsewhere, i.e., training of general skills (e.g., scientific writing) and participating in national and international conferences.

NCA holds the chair of ONWAR and is thus taking the lead in organising PhD student training in neuroscience in Amsterdam (VU, VUmc, NIN, UvA, and AMC) and Rotterdam (Erasmus MC). The committee strongly praised the outstanding leadership of ONWAR by August Smit. ONWAR's course programme is continuously being improved using feedback from the students. There is an annual

PhD student retreat that is organised by the students. This helps them to build their own network and inculcates other skills, such as how to organise a conference.

The PhD committee of NCA did note one weakness of their PhD programme: due to the heterogeneous background of PhD students and their research subjects, it is difficult to organise a scientific training programme for the whole group. They have tried to solve this by customizing the NCA PhD regulations to the needs of clinical and pre-clinical scientists. In addition, they organise an obligatory yearly NCA meeting with review and feedback elements.

# Supervision and the effectiveness of supervision plans

Each student at NCA has a team of supervisors. The students' progress is monitored every year using a progress form. In addition, there is a mentoring system within ONWAR, which functions as a back-up for the supervision teams in case of difficulties.

# Success rate, duration, and exit numbers

Over the years, more than 90% of all PhD students at NCA complete their thesis. This percentage is substantially higher than the mean of 75% in Dutch research schools and the committee was impressed by this high success rate. In the years of this evaluation, the mean duration for completing the thesis was 4.98 years (with a standard deviation of less than 8 months). These numbers were not corrected for part-time appointments, maternity leaves, or other leaves of absence. The regular duration of a PhD project is four years in the Netherlands.

# Guidance of PhD candidates to the job market and career prospects

The team of supervisors guide the students in approaching the labour market. In addition, NCA organises career events and there is an alumni programme that helps to keep track of where the students end up. Of those that graduate, 8 out of 10 pursue a research career, mainly in academia and some in industry (biotech or pharma). The remainder pursue other careers, e.g., consultancy, management, business development. Three years after PhD graduation, around 25% of the graduates are still in science, so the largest drop-out is among early post-docs.

# 3.2 Research integrity policy

The assessment committee considered NCA's research integrity policy and the way in which violations of such integrity are prevented. NCA's research integrity policy looks **outstanding** and is an asset to be proud of. NCA adheres to the Research Guide of the VUmc and the joint research code of the VUmc and Academic Medical Center (AMC; this is the second academic hospital in Amsterdam). The committee had the impression that NCA's culture is very open and as a result, certainly allows for an independent and critical pursuit of science.

The VUmc Research Guide can be found on the NCA website. It provides an overview of the available support for conducting research at VUmc as well as guidelines for adequate data stewardship (including proper data storage). In the majority of NCA laboratories, official laboratory journals are used. Patient data are stored digitally in protected directories according to the regulations for good clinical practice. The committee learned that in the near future, this will be followed by protection of the storage of all digital data. This protected data storage will be used for both experimental and

patient-related data. NCA has three research committees that provide an independent review of the scientific quality of research proposals of investigators. The purpose of this review is to ensure the highest quality of research and to support researchers affiliated to NCA.

# 4. Recommendations

# 4.1 Quality of the research unit

# 1) Strategy in general

The committee recommends that NCA strategically assesses where it wants to be at the time of the next evaluation and beyond. In the past six years, NCA's strategy was focused on promoting interdisciplinary collaboration and translational research. This has been extremely successful. However, other than the focus on translational research, NCA's strategy is driven by the interests of individual researchers and groups. The committee recognised that NCA's overall excellent research quality and much of its success in innovation can be attributed in part to an inspiring culture, in which scientists are encouraged to take risks and have the intellectual freedom to influence the direction of their research. However, a potential limitation of this may be that the NCA lacks enough of a top-down research strategy to maintain programmes at an internationally leading level, and to be able to move rapidly to develop important new areas of research that have not featured in the past at NCA. Looking to the future, the committee believes that NCA will need to manage longer-term research strategies for the whole institute.

The committee encourages NCA to consider which research will be innovative, outstanding, sustainable, and achieve high impact. From this, a more granular 'vision statement' could be distilled that will help guide research groups in setting common objectives. This also will be useful as a guide for planning increased collaboration with the University of Amsterdam (see recommendation 2). As part of this exercise, the committee recommends that NCA also evaluates the balance between fundamental research and translational research to ensure that it contributes best to long term growth. The committee felt that there may be too little focus on basic science at the moment.

# 2) Amsterdam-wide initiatives

The board of deans of VU and VUmc has asked the assessment committee to comment on the plans to intensify neuroscience collaborations with the University of Amsterdam (UvA). However, other than to note that there are areas that could usefully be strengthened (mentioned above), the committee feels it is not possible to comment on these plans because it does not have a comprehensive and informed view of UvA research.

# 3) External advisory board

The committee recommends that NCA establishes an external scientific advisory board. The committee greatly admired the cohesive spirit of the NCA community. However, the committee also feared that this could make NCA somewhat monolithic unless explicit efforts were made for periodic renewal of ideas and staff from the outside. The committee learned that NCA was formerly advised by an independent external scientific committee, but that the board is currently inactive. The committee recommends reviving the advisory board. This board should meet to review progress at least once a year and provide input. Crucially, the board should be encouraged to help NCA identify new opportunities and areas for development. This will help NCA to stay at the forefront of

neuroscience by proactively seizing opportunities and embracing technological and field changes quickly.

# 4) Recruiting and retaining top scientists

The committee recommends that the NCA management takes specific steps to increase the recruitment of international, world-leading scientists. A more general, important concern of the committee is the institute's ability to recruit and retain the most talented scientists, as well as employees with specific skills. The committee feels this constitutes a threat to NCA's viability. This was extensively discussed with NCA's management team during the site visit. The committee recognised a number of challenges (not uncommon to other institutions), but encourages creative approaches to addressing them:

- The number of staff positions is limited, certainly for non-clinical scientists. As a result, the institute has limited funds to recruit and retain world leaders. Most of NCA's talents are funded with personal grants (e.g., ERC) or excellence programmes.
- It is difficult to retain talented postdocs. NCA tries to keep the most talented postdocs on soft money, but this is often not sufficient to keep them long enough to enable them to grow into mature postdocs. A career progression strategy is needed for early-career scientists as they progress to full independence.
- It is difficult for clinical researchers to stay active in research. Although the translational focus of the programmes encourages early research exposure, the demands of combined clinical training and care are high. Many of them perform a medical residency after or while finishing their PhD or, subsequently, need to take on substantial clinical care responsibilities, leaving them very little time for research. This makes it hard to stay at the forefront of science and limits incentives for a clinical academic career. Recruiting and retaining strong clinical researchers to expand the research with the extremely valuable clinical cohorts is essential.
- Non-clinical staff members often have to spend a substantial part of their time on teaching. In some cases, this could risk compromising the ability to compete with international research groups, although some staff members have indicated that teaching is also a great method to recruit talented students. The balance needs to be monitored closely on an individual level.
- Finally, while being impressed by the research quality, the committee also was surprised by the 'Dutch dominance' in NCA's staff, i.e., almost all principal investigators have Dutch nationality. This was discussed with NCA's management team. While there are clear drivers for this, e.g., language barriers particularly for medical doctors who need to speak Dutch, the committee encourages NCA to consider ways of more actively recruiting international scientists. Diversity of backgrounds and outlook will significantly contribute to future strength.

# 5) Structural funding for infrastructure

The committee recommends that NCA explores ways of funding its infrastructure and support staff across programmes to enable long term support for some common advanced infrastructure and staff. The committee learned that it is difficult for NCA to obtain structural funding to maintain its infrastructure (e.g., for maintaining the cohorts, renewal of equipment, and computational facilities). In addition, it is difficult to obtain funding for personnel to support data acquisition, data analysis, and data management. More generally, it appeared sometimes difficult for the institute to retain the so-called 'solid middle group' of key advanced research support staff.

# 6) Industry Alliance Office (IAO)

The committee encourages the IAO to explore possibilities to broaden its own potential. The IAO is unique and it is doing an outstanding job in attracting research funding. In 2013-2014, NCA has acquired a contract portfolio of more than EUR 10 M through the IAO (see Appendix 3, Table 2). The committee strongly praised this initiative, which constitutes a creative solution to the steadily declining amount of direct research funding. However, the committee had the impression that the IAO is self-limiting, in the sense that there ultimately is a limited potential demand from the traditional industry sources being pursued, e.g., the number of phase II trials is limited. The committee encourages the IAO to explore additional possibilities, for instance through exploiting intellectual property rights generated by the patient cohorts or expanding the scope of industry outreach, e.g., for healthcare technology companies. The committee has also discussed issues of data ownership and intellectual property rights with the IAO. The committee thinks it is important to ensure that the value generated from data and intellectual property rights contributes to support of NCA.

# 7) Outreach activities

The committee encourages NCA to make a strong, coordinated effort to sell the 'brand' of excellence at NCA and to involve the public in its activities and support. Although the cohorts associated with NCA are continuously reaching out to the general public, the NCA institute per se seems to perform relatively fewer outreach activities. This might involve recruiting a press officer. Such an effort will help NCA to reach succeeding generations of talented researchers. In addition, involving the whole city of Amsterdam in NCA's mission can help fund raising, recruiting study participants, and getting citizens involved in other ways.

# 8) Therapeutic development

The committee encourages NCA to further promote the translation of its innovative findings in clinical practice. Although the committee praised NCA's outstanding integration of basic science and clinical research, it noticed a relative lack of focus on the development of treatments (i.e., there is more focus on prevention and early detection). Possible initiatives could include:

- a drug discovery programme in specific areas;
- development of a broader range of clinical trial units;
- promoting investigator-initiated trials;
- developing new treatments based on experiences in related disease areas.

# 4.2 PhD programme

1) The committee recommends taking advantage of the unique situation in the Netherlands to market the PhD programme more internationally. This can be used as part of an explicit strategy for growth and renewal. The assessment committee learned that PhD students are employees instead of students in the Netherlands. This should make Dutch PhD programmes highly internationally competitive. NCA has a number of what appear to be particularly good employment benefits for PhD students, such as resources for conferences, courses, thesis printing, and an outstanding training environment. English is spoken throughout the research environment, which should attract non-

English speakers who want to gain language proficiency in the course of their research training. In this sense, the PhD programme seems to be a hidden gem.

- 2) The committee recommends that the university management explores ways of continuing or enhancing the direct funding for PhD supervision. The NCA management team has expressed concerns about the ongoing reduction of direct funding for supervising PhD students. The PhD programme is not completely financially supported by the faculties at the moment. However, as noted above, the committee believes that this training programme should be viewed as a fundamentally important part of the plan for sustainability and growth of NCA.
- 3) The committee learned that in the first month of a PhD project, an ONWAR introduction course includes a visit to various ONWAR-associated research labs, so that students get acquainted with the landscape of neuroscience in Amsterdam and Rotterdam. The committee thinks it would be useful for students to actually work in multiple laboratories, so it might be good to consider lab rotations.

# 4.3 Research integrity

No recommendations were deemed necessary.

# **Appendix 1.** Short CVs of the members of the assessment committee

# Professor Paul Matthews (chairman)

Paul Matthews is head of the Division of Brain Sciences in the Department of Medicine of Imperial College, London. His research is noted for innovative translational applications of clinical imaging for the neurosciences. He was the founding Director of two internationally leading research imaging centres, the University of Oxford Centre for Functional Magnetic Resonance Imaging of the Brain and GlaxoSmithKline's Clinical Imaging Centre. From 2005 - 2014 he was a Vice President of GlaxoSmithKline Medicines Discovery and Development. Amongst many external commitments, Professor Matthews has served two terms on the MRC Neuroscience and Mental Health Board and remains active on several committees. He was a member of the UK HEFCE REF Neuroscience Subcommittee for assessment of Neurosciences, Psychology and related areas; and is a member of the Steering Committees for UK Biobank and for the UK Dementias Platform. Professor Matthews was awarded an OBE in 2008 for services to neuroscience. He was elected to the Academy of Medical Sciences in 2014.

### **Professor Jonathan Flint**

Jonathan Flint is Professor of Molecular Psychiatry, Wellcome Trust Principal Fellow, Group Head / Pl, and Consultant Physician at the Wellcome Trust Centre for Human Genetics, University of Oxford. His laboratory is investigating the genetic basis of psychiatric disorders, in particular the origins of stress related conditions, such as anxiety and depression. Knowing more about the biological basis of these very common disorders could help develop better therapies, and use more efficiently those we already have. His group has studied neuroticism, a personality trait that is a major genetic mediator of depression, in over 900 human families using a personality questionnaire. In addition, they use mice behaviour to help investigate human anxiety and depression. Professor Flint has published numerous publications, and has garnered a significant amount of grant support for his pioneering work. He is moving to a post at UCLA to run a large study of the genetic basis of depression.

### **Professor Jean Marc Fritschy**

Jean Marc Fritschy is Professor for Neuropharmacology at the Institute of Pharmacology and Toxicology, University of Zurich and Director of the Neuroscience Center Zurich. Since August 2015, he is Deputy Dean of the Faculty of Medicine of the University of Zurich. A major topic of his research is the functional organization and plasticity of the GABAergic system, using a multidisciplinary approach ranging from molecular and cell biology to immunoelectron microscopy. His research group works with primary neuronal cultures and transgenic mice. Animal models are essential tools for investigating cellular and molecular alterations contributing to neurological and psychiatric disorders. To this end, they are working with mouse models of temporal lobe epilepsy and neurodegenerative diseases (Alzheimer's and Parkinson), with a specific focus on neuro-immune interactions and the contribution of inflammation to pathophysiology of these brain diseases. He has been co-chief editor of the *European Journal of Neuroscience*, the official journal of the Federation of European Neuroscience Societies, in the period 2008-2014.

# **Professor Andreas Meyer-Lindenberg**

Andreas Meyer-Lindenberg is Director of the Central Institute of Mental Health, as well as the Medical Director of the Department of Psychiatry and Psychotherapy at the Institute, based in Mannheim, Germany. He is also Professor and Chairman of Psychiatry and Psychotherapy at the University of Heidelberg in Heidelberg, Germany. In addition, he is board certified in psychiatry, psychotherapy, and neurology. His research interests focus on the development of novel treatments for severe psychiatric disorders through an application of multimodal neuroimaging, genetics and enviromics to characterize brain circuits underlying the risk for mental illness and cognitive dysfunction.

### **Professor Trevor Smart**

Trevor Smart is the Schild Professor of Pharmacology at University College London and Head of the Department of Neuroscience, Physiology & Pharmacology. He chairs the UCL Neuroscience Research Domain that encompasses ~500 Pls in basic and clinical neuroscience. In 2000, he became an FRPharmS and in 2006 he was made a Fellow of the Academy of Medical Sciences. He is internationally recognised for his contributions to our understanding of the GABAA receptor. His research is focussed on the cellular and molecular physiology and pharmacology of GABAA, glycine and NMDA receptors, which are major inhibitory and excitatory neurotransmitter receptors in the brain, pivotally involved in controlling nerve cell excitability. These receptors feature prominently in neurological diseases, with the GABA receptor being a target for several therapeutic classes of drugs. In addition to his outstanding research record, he has been an editor of *Journal of Physiology* and *Neuropharmacology* and Senior Editor of *Brit. J. Pharmacology*. He has served on the MRC Neurosciences and Mental Health Board and currently sits on the Royal Society Newton Fellowships Panel. He has been previously awarded the Sandoz prize in Pharmacology, the Lilly Award for Pharmaceutical Sciences, the RSPGB Conference Science Medal and in 2012 delivered the biennial Gaddum Memorial Award Lecture.

# **Professor Reisa Sperling**

Reisa Sperling is the Director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital and the Co-Director of the Neuroimaging Core and the Outreach Core of the Massachusetts Alzheimer's Disease Research Center at Massachusetts General Hospital. In addition, she is a Professor of Neurology at Harvard Medical School. Her research is focused on the early diagnosis and treatment of Alzheimer's disease. Dr Sperling has overseen a number of clinical trials of potential disease-modifying therapeutics in early Alzheimer's disease, and currently leads the Anti-Amyloid Treatment in Asymptomatic Alzheimer's disease (A4) Study, the first of its kind prevention trial in clinically normal older individuals with evidence of amyloid accumulation. She is the Principal Investigator of the Harvard Aging Brain Study, and has published over 120 peer-reviewed research articles on memory, aging, and early AD. Dr Sperling is a co-recipient of the 2015 American Academy of Neurology Potamkin Award.

# Dr Linda van den Berg

Linda van den Berg assisted the committee as an external independent secretary. She is a self-employed science writer and communications consultant with a background in biomedical sciences. Her company *Washoe Life Science Communications* offers a variety of communication services to academic institutes and commercial companies.

**Appendix 2.** NCA site visit programme 16&17 November 2015

Time	Day 1: 16 November 2015	Activity
08:30-09:00	Breakfast meeting	Meet & Greet with assessment committee
	Guests: Management Team members: Arjen Brussaard, Philip Scheltens, Brenda Penninx, Dorret Boomsma, August Smit, Johannes de Boer	Science writer (Linda van den Berg) attending
09:00-10:00	Opening session with Scientific Director & Management Team	Introduction Meeting
	Guests: Management Team members: Arjen Brussaard, Philip Scheltens, Brenda Penninx, Dorret Boomsma, August Smit, Johannes de Boer	Science writer attending
9:00	1: Arjen Brussaard	15 minute kick-off
9:15	2: Management Team	Discussion: Q&As
10:00-12:00	Meeting with the Research Programme Leaders	Presentation & Discussion
	Guests: Hugo Vrenken, Johannes de Boer, Huibert Mansvelder, Marjo van der Knaap, Matthijs Verhage, Wiesje van der Flier, August Smit, Joep Killestein, Elga de Vries, Brenda Penninx, Sabine Spijker	Science writer attending
10:00	1: Hugo Vrenken, Huibert Mansvelder, Johannes de Boer	10 minute presentation
10:15	2: Matthijs Verhage, Marjo van der Knaap	10 minute presentation
10:30	3: Wiesje van der Flier, August Smit	10 minute presentation
10:45	4: Elga de Vries, Joep Killestein	10 minute presentation
11:00	5: Sabine Spijker, Brenda Penninx	10 minute presentation
11:15	6: All	Discussion
12:00-13:00	Lunch Break / First Impressions	Closed Meeting
	Only members of External Evaluation Committee	Science writer attending
	Interview Sessions with individual Mid-Career Investigators and selected Group Leaders	Presentations & Discussion
13:00-14:45		Science writer attending
13:00	1: Hugo Vrenken (group leader)	5 minute presentation
13:15	2: Ysbrand van der Werf (team leader)	5 minute presentation
13:30	3: Betty Tijms (mid-career)	5 minute presentation
13:45	4: Henne Holstege (team leader)	5 minute presentation
14:00	5: Odile van den Heuvel (group leader)	5 minute presentation
14:15	6: Meike Bartels (group leader)	5 minute presentation
14:30	7: Danielle Posthuma (head of department)	5 minute presentation
14:45-15:00	Tea Break	
15:00-16:45		Science writer attending
15:00	1: Vivi Heine (team leader)	5 minute presentation
15:15	2: Niels Cornelisse (team leader)	5 minute presentation
15:30	3: Christiaan de Kock (team leader)	5 minute presentation
15:45	4: Ioannis Kramvis (team member – team Meredith)	5 minute presentation
16:00	5: Ronald van Kesteren (team leader)	5 minute presentation
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16:15	6: Jeroen Hoozemans (team leader)	5 minute presentation
16:30	7: Elga de Vries (group leader)	5 minute presentation
17:00-18:30	Break / Open space to study or go online	
	Only members of External Evaluation Committee	
18:30-18:45	Taxi-bus for Committee to restaurant	
19:00-21:30	Dinner Meeting with Deans, Director & Management Team	Working Dinner
	Guests: Johannes Brug (dean VUmc), Peter Beek (dean FBG), Karen Maex (dean FALW/FEW), Arjen Brussaard & Management Team	Informal Discussions with External Evaluation Committee (Q&As) - Science writer attending
21:45-22:00	Taxi-bus for Committee to hotel	
Time	Day 2: 17 November 2015	Activity
9:00-10:00	Pecha Kucha of PhD students	Short Pitches
	Guests: Tinca Polderman (chair) & PhD committee	
9:00	Mohit Dubey	6:40 min presentation
9:08	Anke Hammerschlag	6:40 min presentation
9:16	Claudia Persoon	6:40 min presentation
9:24	Lianne Schmaal	6:40 min presentation
9:32	Alwin Kamermans	6:40 min presentation
9:40	Renske Raaphorst	6:40 min presentation
9:48	Jurre den Haan	6:40 min presentation
10:00-10:30	PhD Committee	Q&A's
	Guests: August Smit, Wiesje van der Flier, Odile van den Heuvel, Bob van Oosten, Arjen Brussaard (chair)	Science writer attending
10:30-11:00	Industry Alliance Office	Q&A's
	Guests: Tim Moser (director business development NCA), Pieter van Bokhoven (business developer NCA), Arjen Brussaard (CSO)	Science writer attending
11:00-12:30	Break / Closed Meeting External Evaluation Committee	Discussion
	Only members of External Evaluation Committee (support of science writer)	Science writer attending
12:30-13:30	Working Lunch Meeting	Q&A's
	Guests: Management Team & Director	Science writer attending
14:00-16:00	Final Closed Meeting External Evaluation Committee	Discussion
	Only members of External Evaluation Committee (support of science writer)	Science writer attending

# Appendix 3. Quantitative data on NCA's composition and financing

Table 1: NCA research staff in number of employees (#) and in full time equivalents (fte)

Total	2009		2010		2011		2012		2013		2014	
	#	fte										
Scientific staff	156	41.03	137	31.90	144	35.30	140	31.15	130	32.88	126	34.73
Post-docs (researchers)	89	41.32	155	76.04	151	73.44	162	67.36	137	56.53	144	60.50
PhD students	168	95.60	153	81.43	168	100.20	154	91.86	172	92.34	181	92.28
Total research staff	413	177.95	446	189.40	463	208.90	456	190.40	439	181.75	451	187.52

Brain Imaging Technology	2013		2014	
	#	fte	#	fte
Scientific staff	25	4.89	23	3.76
Post-docs (researchers)	17	4.98	19	5.36
PhD students	14	7.53	11	6.76
Total research staff	56	17.40	53	15.88
Brain Mechanisms in Health & disease	2013		2014	
	#	fte	#	fte
Scientific staff	31	7.74	27	7.83
Post-docs (researchers)	36	14.61	37	17.27
PhD students	66	35.35	72	35.27
Total research staff	133	57.70	136	60.37
Neurodegeneration	2013		2014	
	#	fte	#	fte
Scientific staff	28	7.89	28	8.78
Post-docs (researchers)	29	11.64	30	10.73
PhD students	38	20.12	38	20.68
Total research staff	95	39.65	96	40.19
Neuroinformation	2013		2014	
Neuroimormation	2013	fte	#	fte
Scientific staff	17	6.15	17	6.45
Post-docs (researchers)	25	15.10	27	16.06
PhD students	23	15.35	22	12.16
Total research staff	66	36.60	66	34.67
Total research stain		30.00	- 00	34.07
Neurobiology of Mental Health	2013		2014	
	#	fte	#	fte
Scientific staff	29	6.21	31	7.91
Post-docs (researchers)	30	10.20	31	11.08
PhD students	30	13.99	38	17.41
Total research staff	89	30.40	100	36.40

Footnote: For the analysis in this section in the category PhD-students, only co-workers that had an employee status as such and conducting research with a primary aim/obligation to graduate were included. External PhD students and MD research staff that also perform PhD thesis research without the obligation to graduate are not included.

**Table 2:** Financial budgets of NCA research in euros.

2009	2010	2011	2012	2013	2014
€	€	€	€	€	€
n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
6,594,300	7,939,262	13,032,708	11,092,777	10,896,213	14,147,550
13,580,420	18,172,132	12,121,152	5,741,757	10,343,102	8,216,186
2,576,000	3,534,291	3,376,520	416,324	2,321,406	11,750,880
22,750,720	29,645,685	28,530,380	17,250,858	23,560,721	34,114,616
	€ n.a. 6,594,300 13,580,420 2,576,000	€ € n.a. n.a. 6,594,300 7,939,262 13,580,420 18,172,132 2,576,000 3,534,291	€       €       €         n.a.       n.a.       n.a.         6,594,300       7,939,262       13,032,708         13,580,420       18,172,132       12,121,152         2,576,000       3,534,291       3,376,520	€         €         €         €           n.a.         n.a.         n.a.         n.a.           6,594,300         7,939,262         13,032,708         11,092,777           13,580,420         18,172,132         12,121,152         5,741,757           2,576,000         3,534,291         3,376,520         416,324	€         €         €         €         €           n.a.         n.a.         n.a.         n.a.         n.a.           6,594,300         7,939,262         13,032,708         11,092,777         10,896,213           13,580,420         18,172,132         12,121,152         5,741,757         10,343,102           2,576,000         3,534,291         3,376,520         416,324         2,321,406

1 = for direct funding, see Table 3; 2 = National Research Council and ERC (European); 3 = all other grant support (from government ministeries to European Committee); 4 = Industry sponsored and/or charitable organizations, in 2013 and 2014 through the Industry Alliance Office.

Brain Imaging	2013	2014
Direct Funding	n.a.	n.a.
Research grants	3,985,000	1,832,108
Consortium grants	150,000	165,000
Industry Alliance	-	485,500
Total funding	4,135,000	2,482,608
Brain Mechanims in Health & Disease	2013	2014
Direct Funding	n.a.	n.a.
Research grants	3,004,746	3,200,000
Consortium grants	2,877,016	1,095,000
Industry Alliance	1,470,000	469,000
Total funding	7,351,762	4,764,000
Neurodegeneration	2013	2014
Direct Funding	n.a.	n.a.
Research grants	1,915,659	7,690,442
Consortium grants	3,393,406	2,046,124
Industry Alliance	615,000	7,706,439
Total funding	5,924,065	17,443,005
Neuroinflammation	2013	2014
Direct Funding	n.a.	n.a.
Research grants	20,000	450,000
Consortium grants	1,551,936	3,412,220
Industry Alliance	-	2,120,998
Total funding	1,571,936	5,983,218
Neurobiology of Mental Health	2013	2014
Direct Funding	n.a.	n.a.
Research grants	1,970,808	975,000
Consortium grants	2,370,744	1,497,842
Industry Alliance	236,406	968,943
Total funding	4,577,958	3,441,785

**Table 3:** Financial expenditure in fte research staff for NCA over the years 2009-2014, and for the research programs over the years 2013-2014.

Total	2009		2010		2011		2012		2013		2014	
	fte	%										
Direct funding	62.5	34.9	69.0	36.4	72.6	34.7	63.8	33.5	63.5	34.9	64.6	34.5
Research grants <sup>1</sup>	39.0	21.8	41.0	21.6	46.7	22.3	48.4	25.4	41.3	22.7	38.7	20.7
Consortium grants <sup>2</sup>	63.0	35.2	68.0	35.9	81.1	38.8	70.2	36.9	69.2	38.1	77.5	41.4
Industry Alliance <sup>3</sup>	14.7	8.2	11.4	6.0	8.6	4.1	8.0	4.2	7.7	4.2	6.6	3.5
Total funding	179.2	100.0	189.4	100.0	209.0	100.0	190.4	100.0	181.8	100.0	187.5	100.0

1 = National Research Council and ERC (European); 2 = all other grant support (from government ministeries to European Committee); 3 = Industry sponsored and/or charitable organizations, in 2013 and 2014 through the Industry Alliance Office

Brain Imaging	2013		2014	
	fte	%	fte	%
Direct Funding	8.5	48.9	6.7	42.4
Research grants	4.0	23.0	2.6	16.6
Consortium grants	3.0	17.2	4.8	30.2
Industry Alliance	1.9	10.9	1.7	10.7
Total funding	17.4	100.0	15.9	100.
Brain Mechanims in Health & Disease	2013		2014	
	fte	%	fte	%
Direct Funding	20.8	36.0	17.9	29.6
Research grants	20.6	35.7	21.7	35.9
Consortium grants	15.6	27.0	20.5	33.9
Industry Alliance	0.7	1.2	0.4	0.7
Total funding	57.7	100.0	60.5	100.
Neurodegeneration	2013		2014	
	fte	%	fte	%
Direct Funding	12.8	32.2	13.8	34.3
Research grants	5.1	12.8	3.6	9.0
Consortium grants	21.8	54.9	22.8	56.7
Industry Alliance	0.0	0.0	0.0	0.0
Total funding	39.7	100.0	40.2	100.
Neuroinflammation	2013		2014	
	fte	%	fte	%
Direct Funding	9.6	26.2	10.8	31.2
Research grants	1.9	5.2	4.0	11.6
Consortium grants	23.3	63.7	18.5	53.5
Industry Alliance	1.8	4.9	1.3	3.8
Total funding	36.6	100.0	34.6	100.0
ar 1:1 fag : III lil	2042		204.4	
Neurobiology of Mental Health	2013	0/	2014	0/
Disast Funding	fte	%	fte	% 42.2
Direct Funding	11.8	38.7	15.4	42.3
Research grants	9.8	32.1	6.8	18.7
Consortium grants	5.5	18.0	10.9	29.9
Industry Alliance	3.4	11.1	3.3	9.1
Total funding	30.5	100.0	36.4	100.

Appendix 4. Explanation of the categories utilised

Category	Meaning	Research quality	Relevance to society	Viability		
1 World leading/ excellent		The research unit has been shown to be one of the few most influential research groups in the world in its particular field.	The research unit makes an outstanding contribution to society.	The research unit is excellently equipped for the future.		
2	Very good	The research unit conducts very good, internationally recognised research.	The research unit makes a very good contribution to society.	The research unit is very well equipped for the future.		
3	Good	The research unit conducts good research.	The research unit makes a good contribution to society.	The research unit makes responsible strategic decisions and is therefore well equipped for the future.		
4	Unsatisfactory	The research unit does not achieve satisfactory results in its field.	The research unit does not make a satisfactory contribution to society.	The research unit is not adequately equipped for the future.		

Source: Standard Evaluation Protocol 2015 - 2021