Amsterdam UMC
University Medical Centers

Amsterdam Neuroscience
Annual Report 2020

Colophon

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Word from the directors

The Resilience of Team Science

In February 2020, Diederik van de Beek was on the phone with biotech companies, alerting them to the new SARS-CoV-2 virus (what we now call COVID-19) and asking them to consider repurposing their work and innovations in the fight against it. Around the same time we, in the Amsterdam Neuroscience office, were pondering what the research institute's central theme for 2020 would be. With our new year's resolution of continuing to find new ways to work together still fresh in our minds, we decided upon Team Science. We had no way of knowing just how spot on that concept – and just how great the need for it – would be within a short matter of months.

Around March 13, the first wave of COVID-19 patients hit our hospital and all research was brought to a halt by the lockdown of our labs and offices. Within two weeks, we shifted gears and our focus was directed towards the specific problems of that time: How can we contribute to COVID-19-related care and knowledge? And: What can we do to help fight the global pandemic?

The following months saw a flurry of activity. Diederik and his team took the lead in a clinical trial in the ICU and set up the Amsterdam UMC COVID-19 Biobank; and the Amsterdam Neuroscience team joined the newly formed COVID-19 Task Force Research, which was responsible for coordinating all COVID-19 research activities within Amsterdam UMC. It was Team Science all right, but just not the kind we had expected.

As the year progressed, we wondered how the COVID-19 pandemic would affect our investigators' research and funding acquisitions. Interesting enough the preclinical and translational investigators of Amsterdam UMC, Vrije Universiteit Amsterdam (Center for Neurogenomics and Cognitive Research), and University of Amsterdam (Swammerdam Institute for Life Sciences) had instantly moved towards a work-from-everywhere-mode from the onset of Q2 onwards. And even grant acquisitions remained at a remarkably high level. With three ERC, three Veni and three Vidi grants and a cumulative total of 55 million euros of conditional research-funding, Amsterdam Neuroscience hit the usual benchmark thresholds. PhD projects continued (following COVID-19 regulations) as did PhD defenses (be it in an online setting). And our researchers managed to keep publishing their work, almost unimpaired and with the usual high impact.

Towards the end of Q3, we organized an online live stream of the Annual Meeting for around 500-600 colleagues. The complete production was broadcast on October 2, to positive reviews. Two months later we took part in the Amsterdam UMC & COVID-19 research event, 'Unorthodox Teams, Accelerating Science', which had more than 1,000 'live' viewers and around 12,000 hits later-on. Unusual metrics, but refreshing and rewarding ones nonetheless.

As 2020 drew to a close, we looked back at, what had proved to be, an incredibly intense year. A year of team efforts. A year of contemplation that also brought an optimistic outlook for the near future. A year where all our researchers and clinicians worked tirelessly around the clock in unchartered waters against an unprecedented virus. And we're so proud of them all. It was, without a doubt, a year of Team Science. A year in which we had been resilient. And with that in mind, we thought: Why not stick to that and pick Resilience as the central theme for 2021.

It is with great pleasure we present our fifth Annual Report. We hope you enjoy reading the results.

Arjen Brussaard – director
Diederik van de Beek – co-director

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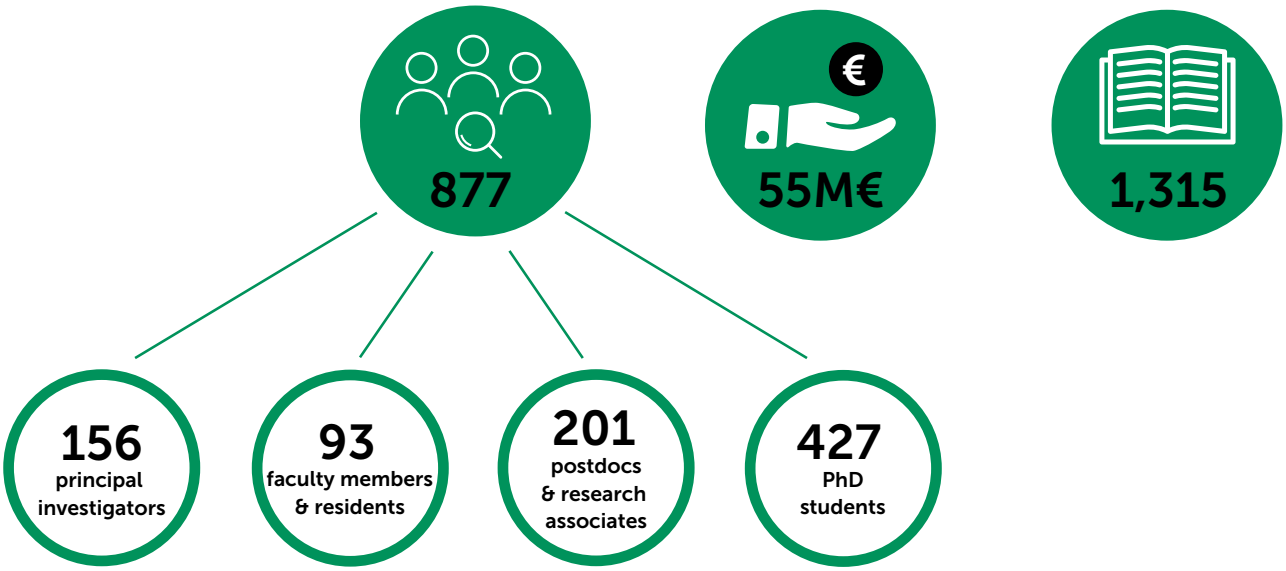
Executive summary

- The collective 'community' of the Amsterdam Neuroscience research institute is currently made up of 877 investigators. This includes 156 principal investigators, 93 faculty members & residents, 201 postdocs & research associates, and 427 PhD students.
- Over the course of 2020, Amsterdam Neuroscience investigators acquired over 55 million euros in conditional funding. This included three Veni grants and three Vidi grants, as well as other major grants from Dutch agencies and the European Commission (EC), including three ERC grants.
- This also included more than 23 million euros from non-profit (patient-oriented) organizations and around 13 million euros funding in contracted research from the biotechnology and pharma industry.
- In 2020, a total of 1,315 refereed articles were published with 175 papers in the highest impact journals (impact factor > 10), and another 354 with a solid impact factor (> 5 < 10).
- Of these 1,315 unique papers, 152 had 'shared' co-authorship (i.e. 'bilocation' affiliations).
- Highlights throughout 2020 include the start of large consortia like the 'Don't be late' consortium under supervision of Hanneke Hulst and the COVID-19 Biobank by Diederik van de Beek. Christiaan Vinkers, Betty Tijms and Camiel Boon are our newest Vidi laureates, in addition Jeanne Savage, Anita van Loenhoud and Aishu Parthasarathy received a Veni grant. ERC grants were awarded to Matthijs Brouwer, Martijn van den Heuvel (both ERC Consolidator grants) and Rik Ossenkoppele (ERC Starting grant).



About Amsterdam Neuroscience

Amsterdam Neuroscience is the research institute for neuroscience of Amsterdam UMC and the science faculties of Vrije Universiteit Amsterdam and the University of Amsterdam. Researchers and clinicians from these three institutions join forces in the field of fundamental, translational and clinical brain research. This collaboration strengthens the scientific excellence in this area, making Amsterdam Neuroscience one of the largest neuroscience communities in Europe.

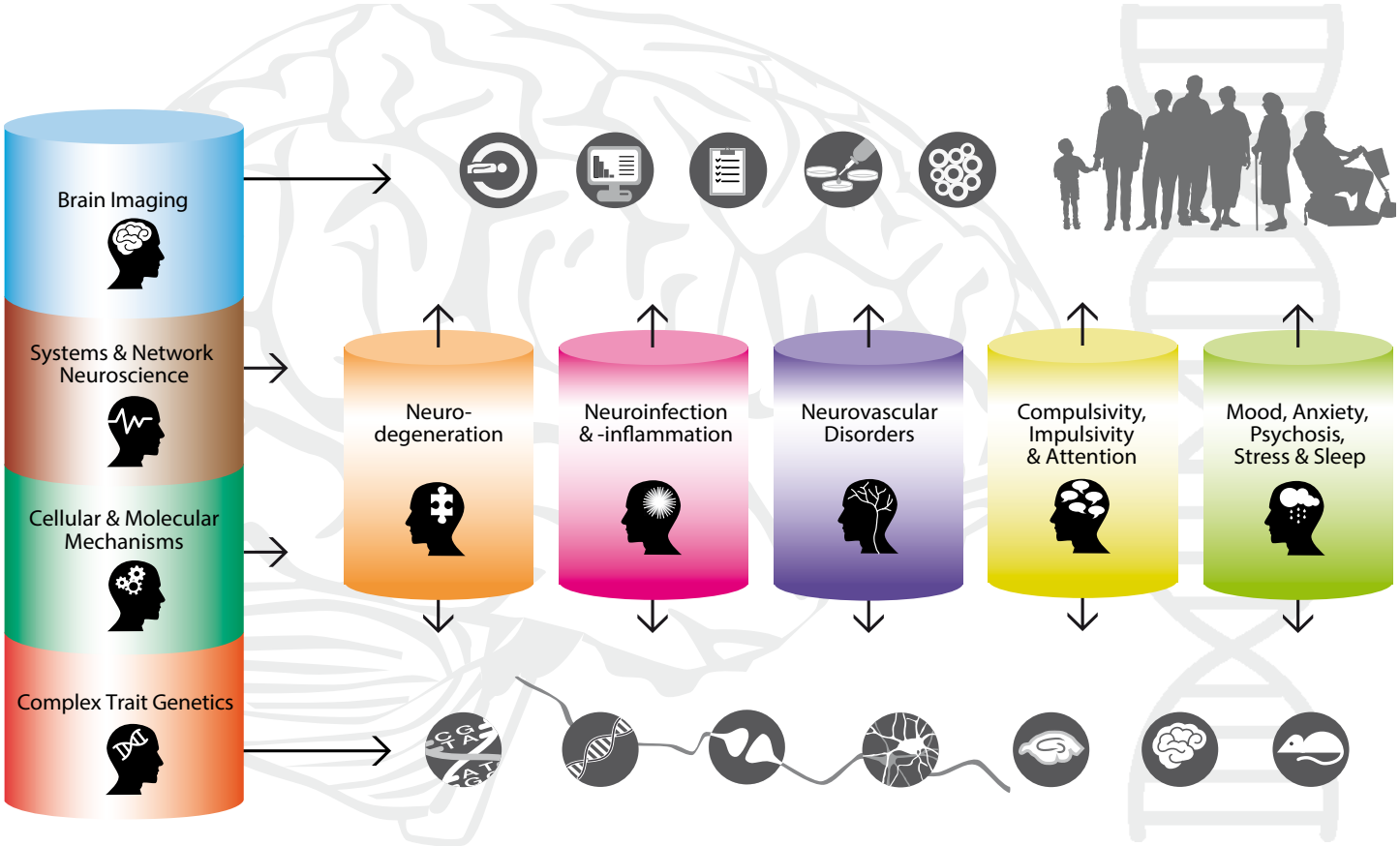
To enable translational neuroscience research, we develop and translate neuroscience knowledge into applications for patients. Amsterdam Neuroscience focuses on scientific excellence, young talent and innovation in four cross-disciplinary research programs. In addition, there are five clinical research programs that focus on both existing and new treatments for a number of brain and nervous system diseases, including neurological, neurovascular and psychiatric disorders.

Amsterdam Neuroscience's overall mission is to broaden the fundamental knowledge of the human brain and nervous system, and to translate this into effective therapies and treatments for the individual patient.

With a focus on both fundamental and translational neuroscience, we work on the primary function of the brain and the underlying cellular and molecular mechanisms. In addition, however, we also identify relevant biomarkers, drug targets and new molecular structures for the purpose of interventions for brain disorders. Through clinical trials on patients, we validate new diagnostic tests, therapies and interventions. The clinical research often focuses on the prevention of brain and nerve disorders, or the recovery thereof. We do this both by investor generated research and through collaborations with external parties such as biotechnology or pharmaceutical companies. Cooperation with industrial partners can, in turn, help accelerate clinical development and validation of new methods and interventions. And all of this while putting the interests of the patient first.

Through scientific excellence and high clinical standards, we provide the best breeding ground for the next generation of neuroscientists, neurologists and psychiatrists. Team science and communication are important core values that make Amsterdam Neuroscience 'the' connecting research institute, where principal researchers contribute to a good infrastructure with partnerships, suitable financing and valorization opportunities.

Research programs



Infographics of the research organization of Amsterdam Neuroscience in the period 2019-2021

Brain Imaging (bi)
Systems & Network Neuroscience (snn)
Cellular & Molecular Mechanisms (cmm)
Complex Trait Genetics (ctg)

Neurodegeneration (nd)
Neuroinfection & -inflammation (nii)
Neurovascular Disorders (ndis)
Compulsivity, Impulsivity & Attention (cia)
Mood, Anxiety, Psychosis, Stress & Sleep (mapss)

Amsterdam Neuroscience

Governance

Management team

Arjen Brussaard (director)	Amsterdam UMC – location VUmc
Diederik van de Beek (co-director)	Amsterdam UMC – location AMC
Susanne la Fleur	Amsterdam UMC – location AMC
Paul Lucassen	University of Amsterdam
Brenda Penninx	Amsterdam UMC – location VUmc
Yolande Pijnenburg	Amsterdam UMC – location VUmc
Guus Smit	Vrije Universiteit Amsterdam
Taco de Vries	Amsterdam UMC – location VUmc
Guido van Wingen	Amsterdam UMC – location AMC

Board of deans

Chris Polman	Dean Amsterdam UMC – location VUmc
Hans Romijn	Dean Amsterdam UMC – location AMC
Guus Schreiber	Dean Faculty of Science, Vrije Universiteit Amsterdam
Peter van Tienderen	Dean Faculty of Science, University of Amsterdam

Program leaders & taskforce members

Brain Imaging

Program leaders	
Dick Veltman	Amsterdam UMC – location VUmc
Liesbeth Reneman	Amsterdam UMC – location AMC
Taskforce members	
Fleur van Rootselaar	Amsterdam UMC – location AMC
Bart van Berckel	Amsterdam UMC – location VUmc

Systems & Network Neuroscience

Program leaders	
Huibert Mansvelder	Vrije Universiteit Amsterdam
Helmut Kessels	University of Amsterdam
Taskforce members	
Johannes de Boer	Vrije Universiteit Amsterdam
Rick Schuurman	Amsterdam UMC – location AMC

Cellular & Molecular Mechanisms

Program leaders	
Matthijs Verhage	Vrije Universiteit Amsterdam
Susanne la Fleur	Amsterdam UMC – location AMC
Taskforce members	
Marjo van der Knaap	Amsterdam UMC – location VUmc
Eric Reits	Amsterdam UMC – location AMC

Complex Trait Genetics

Program leaders	
Danielle Posthuma	Vrije Universiteit Amsterdam
Frank Jacobs	University of Amsterdam
Taskforce members	
Tinca Polderman	Vrije Universiteit Amsterdam
Karin Verweij	Amsterdam UMC – location AMC

Neurodegeneration

Program leaders

Wiesje van der Flier	Amsterdam UMC – location VUmc
Rob de Bie	Amsterdam UMC – location AMC

Taskforce members

Charlotte Teunissen	Amsterdam UMC – location VUmc
Lars van der Heide	University of Amsterdam
Wilma van de Berg	Amsterdam UMC - location VUmc

Neuroinfection & -inflammation

Program leaders

Joep Killestein	Amsterdam UMC – location VUmc
Matthijs Brouwer	Amsterdam UMC – location AMC

Taskforce members

Elga de Vries	Amsterdam UMC – location VUmc
Filip Eftimov	Amsterdam UMC – location AMC

Neurovascular Disorders

Program leaders

Jonathan Coutinho	Amsterdam UMC – location AMC
Dagmar Verbaan	Amsterdam UMC – location AMC

Taskforce members

Gert Kwakkel	Amsterdam UMC – location VUmc
Charles Majoie	Amsterdam UMC – location AMC

Compulsivity, Impulsivity & Attention

Program leaders

Odile van den Heuvel	Amsterdam UMC – location VUmc
Dirk Jan Smit	Amsterdam UMC – location AMC

Taskforce members

Taco de Vries	Amsterdam UMC – location VUmc
Conrado Bosman	University of Amsterdam

Mood, Anxiety, Psychosis, Stress & Sleep

Program leaders

Sabine Spijker	Vrije Universiteit Amsterdam
Christiaan Vinkers	Amsterdam UMC – location VUmc

Taskforce members

Lieuwe de Haan	Amsterdam UMC – location AMC
Aniko Korosi	University of Amsterdam

Research staff

About the metrics

To be able to draft the metrics of our research institute we followed the Standard Evaluation Protocol of 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). As for funding categorization for the university medical centers we used the Netherlands Federation of University Medical Centres (NFU) criteria. In the ratio-conversion from personnel to the full-time-equivalent (fte) spend on research the default (HRM-SAP instructed) guidelines can be applied: full professor: 0.1-0.2 fte; strategic professor: 0.1 fte; associate professor: 0.4 fte; assistant professor: 0.4; investigator: 0.8 fte; postdoc: 0.8 fte; PhD student: 0.75 fte

Amsterdam Neuroscience – Research institute

The collective 'community' of the Amsterdam Neuroscience research institute is currently made up of 877 investigators. This includes 156 principal investigators, 93 faculty members & residents, 201 postdocs & research associates, and 427 PhD students.

Amsterdam Neuroscience – Research programs

Shown here are affiliations categorized by research program of all personnel including PhD students as well as the metrics for PhD students only. Double affiliations were allowed.

All personnel	**Persons**								
	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
Subtotal	111	58	225	73	179	142	76	120	90

PhD students only	**Persons**								
	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
Subtotal	55	19	137	32	70	72	37	70	35

Funding

Amsterdam Neuroscience – Research funding

Shown here is the grand total, the subtotals per type of funding as well categorized per research program of newly acquired funding for the institute. In this table funding that is unique to each particular research program is quoted. Double affilations are not shown.

	Grand total	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
Total	€ 55,337,353	€ 4,609,550	€ 1,614,398	€ 5,894,371	€ 3,842,748	€ 18,151,277	€ 8,811,804	€ 3,118,457	€ 1,855,320	€ 7,439,428

Conditional funding

	Subtotal	bi	snn	cmm	ctg	nd	nii	ndis	cia	mapss
2e geldstroom	€ 18,449,232	€ 343,072	€ 446,652	€ 1,695,704	€ 1,287,843	€ 6,431,234	€ 2,606,456	€ 259,000	€ 636,706	€ 4,742,565
3e geldstroom	€ 23,774,947	€ 3,687,765	€ 854,828	€ 3,679,355	€ 2,213,021	€ 5,020,705	€ 3,377,525	€ 1,620,607	€ 624,278	€ 2,696,86
4e geldstroom	€ 13,113,174	€ 578,713	€ 312,918	€ 519,312	€ 341,884	€ 6,699,338	€ 2,827,823	€ 1,238,850	€ 594,336	€ -

NFU definition

- "2e geldstroom": conditional funding by intermediary public bodies and agencies (ZonMw, NWO, KNAW and the EU);
- "3e geldstroom": private funding by non-profit organizations;
- "4e geldstroom": private funding from commercial sources: contract-research and clinical trial research funded by biotech and pharma industry and acquired by the Industry Alliance Office (IAO).

Research output & quality

Amsterdam Neuroscience – Research output

Shown here are the metrics for all types of publications. Double affiliations are not shown, i.e. each publication in this table is only affiliated with one research program.

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

Notes on the distinct categories (according to the latest SEP protocol):

1. Articles in journals that are non-refereed, yet deemed important for the field;
2. Publications aimed at professionals in the public and private sector (professional publications), including patents and annotations (e.g. law);
3. Also known as "populariserende artikelen";
4. Other types of research output (if applicable), such as abstracts, patents, editorships, inaugural lectures, designs and prototypes (e.g. engineering) and media appearances.

High-impact publications

A total of 1,315 refereed papers were written in 2020 by Amsterdam Neuroscience researchers. Out of this, total 354 papers were published in international journals with an impact factor of between 5 - 10, and 175 papers were in journals with an impact factor of 10 or higher. Of the latter category, at least 30 papers were original research papers in the center of our core strategy and with first and last authors coming from our organization. There were an additional 27 papers that were published as so-called perspectives and reviews in high-impact journals (i.e. > 10), with corresponding authors from our institute. Another 19 papers were published in international journals with an exceptionally high impact factor of over 20.

Bilocation authorships

In 2020, there were at least 152 'bilocation' papers (i.e. papers in which either VUmc and/or AMC shared co-authorship with university co-authors) written by Amsterdam Neuroscience researchers. VUmc had co-authors on 116 of these papers, while AMC participated on 70 bilocation papers. With regards to the universities' contribution to these bilocation papers, the VU contributed to 69 and the UvA contributed to 20.

Societal impact

The Amsterdam Neuroscience researchers promote high-class research output. But with the aim to understand the functioning of the human brain and nervous system, and the focus on the translation into effective therapies and treatments for the individual patients, Amsterdam Neuroscience also highly values societal impact. Our societal impact can be understood as stimulating valorization, boosting interdisciplinary collaborations, creating and maintaining societal awareness, and bridging the gap between fundamental and more clinical oriented research results and its implementation. More information about the impact of our research is illustrated in the section of news items of 2020, listed in the second part of this Annual Report 2020.

Digital Annual Meeting 2020

Recap of the Amsterdam Neuroscience Annual Meeting 2020

On October 2, 2020 the fifth Annual Meeting of the Amsterdam Neuroscience research institute took place. During this day around 500 online participants joined this virtual Annual Meeting. With a variety of sessions Amsterdam Neuroscience informed participants on the latest research developments in neuroscience all revolving around this year's theme: team science.

Word of Welcome and Research Reports

Directors of Amsterdam Neuroscience Arjen Brussaard and Diederik van de Beek opened this year's Annual Meeting together with the host Kim Coppes. They highlight the overarching theme of 2020 and launch the new MAGAZINE 2020. Followed by presentations of four young researcher *Gijs Kooij* (Assistant Professor Molecular cell biology and Immunology), *Marc Engelen* (Pediatric Neurologist), *Linda Douw* (Associate Professor Anatomy & Neurosciences), and *Mirjam van Zuiden* (Assistant Professor Psychiatry). These researchers also spoke about research opportunities, funding and collaborations.

Swammerdam Lecture

This year's Swammerdam lecture was given by *Hilgo Bruining*, supported by his colleagues *Klaus Linkenkaer-Hansen*, *Niels Cornelisse*, and *Bas Stunnenberg*. Hilgo Bruining is an associate professor and child and adolescent psychiatrist at Amsterdam UMC. His presentation was entitled 'Transforming treatments for neurodevelopmental disorders into solid N-of-1 trials'. A paradigm shift from one-size-fits-all to a tailored and personalized approach is urgently needed. Hilgo Bruining outlined how the NWA supported NewTDec consortium takes on this challenge to inform, perform and monitor rational treatments at the patient 'n-of-1' level. The consortium exemplifies team science focused at the integration of various model-driven and data-driven approaches needed for precision therapy in neurodevelopmental disorders. At the end of the session Hilgo Bruining and his colleagues revealed the name of their neurodevelopmental precision center: *N=You* Neurodevelopmental Precision Center.

Pecha Kucha Presentations

Junior and mid-career neuroscience researchers presented their research during the Pecha Kucha competition led by postdoctoral researcher Priyanka Rao. Selected from the nine research programs of Amsterdam Neuroscience *Esther Visser*, *Shu Liu*, *Kitty Reemst*, *Dirk Jan Ardesch*, *Hanna Lammertse*, *Naomi Buntsma*, *Anke Dijkstra*, and *Tommy Broeders* told their scientific story in the familiar Pecha Kucha format. At the end of the session, the audience voted for the best Pecha Kucha presenter of 2020. Congratulations to *Dirk Jan Ardesch* who won with his presentation 'Human brain evolution: How special are we?'.

Selection of news items of 2020

New insights on Aβ independent regulators of tau pathology in Alzheimer disease

In a great collaboration between the Center for Neurogenomics and Cognitive Research and the Alzheimer Center Amsterdam, Rik van der Kant and Rik Ossenkoppele - both affiliated with Amsterdam Neuroscience - published a review on amyloid-β-independent regulators of tau in Alzheimer disease.

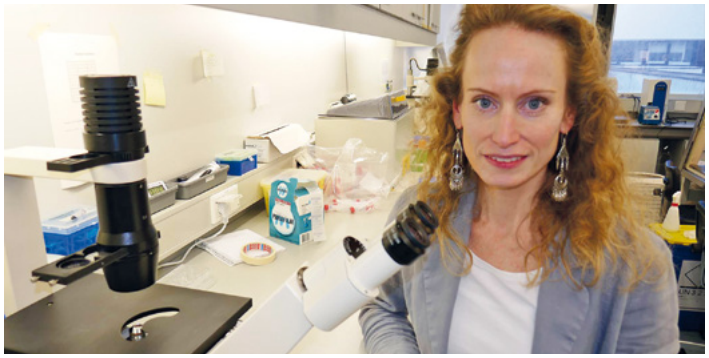
Rik van der Kant

Rik van der Kant (Vrije Universiteit Amsterdam, Amsterdam UMC) and his colleagues Larry Goldstein (University of California San Diego) and Rik Ossenkoppele (Amsterdam UMC, University of Lund Sweden) published a review in Nature Reviews Neuroscience with new insights on the Alzheimer disease (AD) pathology. In their review, they summarize how accumulation of amyloid-β (Aβ) plaques precedes tau neurofibrillary tangle in AD patients. “The correlation between Aβ and tau is often interpreted as causation, where Aβ is considered the main driver of tau pathology and neurodegeneration in AD,” says Van der Kant. In the review, the authors highlight a number of pathways that drive tau protein accumulation independently of amyloid. For example, Van der Kant and his colleagues review evidence showing that tau accumulation can be due to disturbed cholesterol metabolism, endosomal transport, microglial activation. Cholesterol for example directly regulates degradation of tau, and is of particular interest as novel brain-cholesterol targeting drugs that have recently been discovered.

More than 1.2 million euros for stem cell research into neuronal abnormalities in white matter disorders

Associate professor of pediatric neurology of Amsterdam UMC Dr. Vivi Heine receives a grant from the EU Joint Program on Rare Diseases (EJP RD). Heine receives this grant of more than 1.2 million euros together with four leading European laboratories in the field of induced pluripotent stem cell (iPSC) technology and functional analysis of neuronal activity. The research project called NG4Leuko will explore complex neuron-glia interactions in the brains of patients with white matter disorders.

Recent insights suggest that in addition to white matter and myelin, nerve cells and their functions are damaged in patients with various white matter disorders. The research of Heine and



Vivi Heine

her colleagues will focus specifically on the involvement of these nerve cells in white matter abnormalities in patients. An innovative approach will be used: modern - OMICS and functional activity measurements will be combined with advanced 2D and 3D iPSC and organoid models.

The immuno-metabolic depression model: towards dissection of depression’s heterogeneity and matched ‘precision psychiatry’ treatment

Depression is highly prevalent and is the second leading contributor to disability worldwide. This underlines the need for insights in the dysregulated biological pathways and the search for suitable personalized treatment. Assistant professor Yuri Milaneschi and professor Brenda Penninx from the department of Psychiatry of Amsterdam UMC, highlight the future of the immune-metabolic depression model in their joint review published in the journal Biological Psychiatry.

Yuri Milaneschi

Yuri Milaneschi and his colleagues describe the immuno-metabolic depression model in their review. This model explains how immuno-metabolic dysregulations vary as a function of depression heterogeneity. It firstly illustrates that such biological dysregulations map more consistently to ‘atypical’ behavioral symptoms reflecting altered energy intake/expenditure balance (strong sensation of hunger, weight gain, hypersomnia, fatigue and the sensation of heavy limbs). Secondly, it shows that these biological dysregulations may moderate the antidepressant effects of standard or novel (e.g. anti-inflammatory) therapeutic approaches. The immune-metabolic depression dimension described in the

review could be used to dissect depression's heterogeneity and has the potential to match group of patients to specific treatments with higher likelihood of clinical success, which are essential steps towards 'precision psychiatry'.

Alzheimer Centrum Amsterdam is allowed to kickstart clinical study on early onset AD gen

The Alzheimer Center Amsterdam is allowed to start a new clinical study among people with a genetic mutation that leads to Alzheimer's disease (AD). The Central Committee on Research Involving Human Subjects (CCMO) has given permission for this research. Prof. Philip Scheltens, director of Alzheimer Center Amsterdam, and Jetske van der Schaar, carrier of this AD gene, are extremely happy with this news.

Jetske van der Schaar

The new Alzheimer Center research is part of the Dominantly Inherited Alzheimer Network (DIAN), led by Washington University in St. Louis (MO). In this study, participants with a high risk for AD are followed. Participants either carry a dominant gene mutation that 100% certain leads to the development of AD, at a relatively young age, or participants are member of a family in which this gene is present resulting in a 50% chance of AD. Participants are followed to determine how the disease develops over time. After a while, they will also join an intervention study with medication directed against the Tau protein. Scheltens: "We strive to treat AD and hope to prevent the condition in the long term. The research is based on the idea that changes in the brain are well ahead of the AD symptoms."

2019: A year of significant growth at the Industry Alliance Office

In 2019, the Industry Alliance Office (IAO) that supports the Amsterdam Neuroscience research institute with the acquisition of contract research for drug discovery, development, and diagnostics, acquired a total of > 10 M € in new research contracts sponsored by biotech and pharma companies from all over the world. This is an increase of 55% compared to 2018, and mainly due to the renewal and expansion of a great Business Development team.

It concerns a total of > 45 new contracts, ranging in value from 20,000 € to 1.94 M €. At location VUmc of Amsterdam UMC there was a distribution of IAO contracts with 50% in the domain of Alzheimer's disease and dementia and 30% on multiple sclerosis and 20% on other disease indications. At the location of AMC, contracts in 2018 and 2019 were mainly on Parkinson's disease, meningitis, stroke and other disease indications. Projects include, but are not limited to, the development of novel delivery methods of biologicals across the blood brain barrier, implementation of new PET ligands for measuring changes in synaptic density in patients, implementation of new liquid biomarkers for treatment response in cohort studies and clinical trials, and testing the first gene therapy interventions for Alzheimer's disease. The aim for 2020 is to achieve an even more balanced distribution among the various indications. The IAO also safeguards a solid balance between preclinical, translational and clinical research.

Pieter van Bokhoven

Sasja Heetveld

Dilek Iusuf

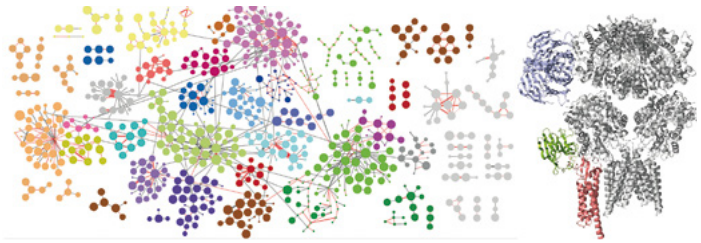
Prisca Leferink

Sanne Stembert

Stitching the Synapse

A new study by Miguel Gonzalez- Lozano and colleagues of the CNCR at VU Amsterdam demonstrates how cross-linking mass spectrometry can contribute to the discovery of novel synaptic protein interactions. The study was published with high impact in Science Advances on February 19, 2020 (IF > 12).

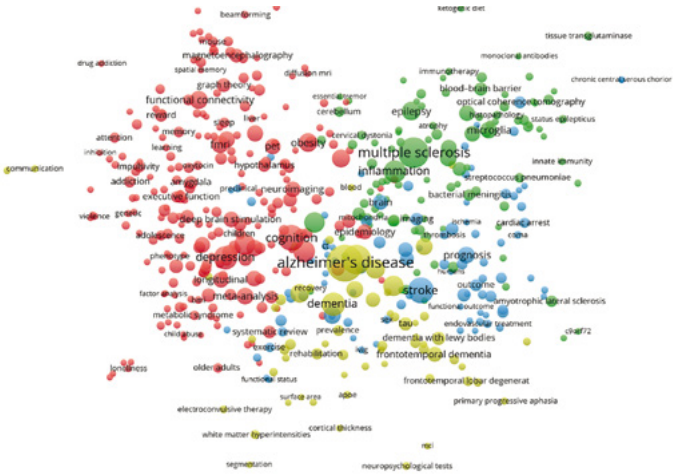
Synaptic transmission requires functionally specialized molecular machineries constituted by a multitude of interacting synaptic proteins. In this study the researchers made use of recent advances in cross-linking mass spectrometry (XL-MS) in combination with biochemical and computational approaches to reveal the architecture and assembly of synaptic protein complexes from mouse brain hippocampus and cerebellum. The 12.000 unique lysine-lysine cross-links comprise connections within and between 2,362 proteins. This extensive collection was the basis to identify novel protein partners, to model protein conformational dynamics and to delineate within and between protein interactions of main synaptic constituents, such as CAMK2, the AMPA-type glutamate receptor and associated proteins. Using various biochemical and computational approaches, we validated the fidelity of our procedure and investigated protein interactions and dynamics for key synaptic proteins, such as CAMK2 and the AMPA receptor. This extensive resource provides a novel perspective on protein structures, assemblies and interactions of the synaptic proteome. This protein interaction resource is easily accessible via a web-based platform to provide new entries into exploration of all protein interactions.



Power of collaboration

Amsterdam Neuroscience performed a connectomics analysis of all publications affiliated with the Amsterdam Neuroscience research institute and published in the period 2016-2018. Rik Iping (consultant) and Arjen Brussaard are reporting these analyses.

On the basis of the metadata of the more than 3600 publications affiliated with Amsterdam Neuroscience, published during the period between 1 January 2016 and and 31 December 2018, the so-called connectomics plots (or networks) were visualized on the basis of co-author relationships and use of keywords in these publications.

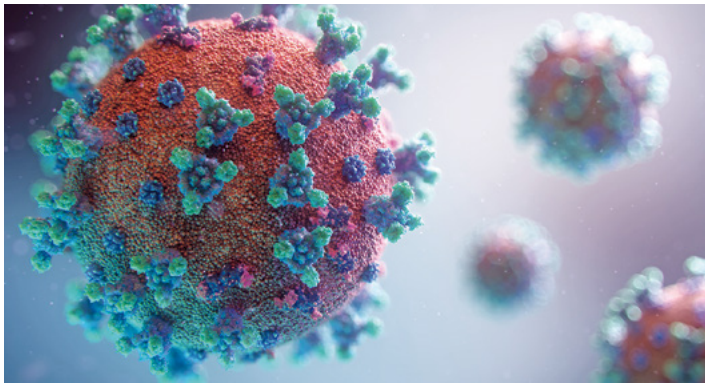


Using VOSviewer software, and by downloading the bibliographic data from EuropePMC for this set of Digital Object Indentifiers (DOI´s), we proceeded and completed an analysis of the Amsterdam Neuroscience institute. The results show the connectomics plot of Amsterdam Neuroscience (corresponding) authors with at least fifteen (but no more than 50) co-authoring publications over the period 2016-2018. In addition, we show a keyword network and research topics word cloud. Again, size of spheres is equivalent to number of publications in which a particular keyword was indicated, the color coding is a proxy of the overlap of different key words used in the same publication. The connectomics plots show the power of collaboration in our research institute.

Amsterdam UMC starts clinical study amongst COVID-19 patients

The research teams of doctor Alexander Vlaar and professor Diederik van de Beek join forces on a randomized clinical trial in severe COVID-19 pneumonia at Amsterdam UMC.

Researchers at Amsterdam UMC have just started a randomized clinical trial for critically ill patients with COVID-19 who have been admitted to intensive care with severe pneumonia.



The new study set up in close collaboration by the sponsor InflaRx, a German biopharmaceutical company, and the teams of doctor Alexander Vlaar and professor Diederik van de Beek examines the safety and effectiveness of a treatment with an antibody that blocks inflammatory factor C5a. This inflammatory factor is part of an important defense mechanism against the virus, the complement system, however in some cases it causes an excessive inflammation. By switching off C5a the damage by the inflammatory response might be prevented. A recent submitted study report (preprint) showed a promising suppressive effect when two Chinese patients were treated with the same anti-C5a monoclonal antibody.

Neurological symptoms in COVID-19 patients: an update

In serious cases of corona, SARS-CoV-2 enters the lungs, which results in lasting damage of the lungs. However, the virus, or the body's response to it, can injure other organs as well. Scientists are just performing research on the scope and nature of that harm. After the COVID pandemic hit the Netherlands it became clear that various other organs than the long may also be affected, and it appeared that neurological symptoms were seen in around one third of the COVID-19 patients of Amsterdam UMC. What were the indications in those days that the brain was affected in COVID-19 diseased patients? Suzanne Geerlings, infectious disease specialist at Amsterdam UMC, shared her knowledge on this topic.

Suzanne Geerlings

One of the striking set of symptoms in COVID-19 patients centers on the brain and central nervous system. Suzanne Geerlings believed that neurologists were needed to assess coronavirus patients: "We must learn from our patients in the acute phase of the disease. For example, which subgroup has an increased risk of these neurological manifestations and needs more monitoring and evaluation. A prospective cohort with a follow-up in the post COVID-19 outpatient clinic can help us to give more insight into the pathogenesis and hopefully also in prevention and treatment possibilities, because the manifestations can be very severe and even lead to death."

Intensivists had seen patients with encephalitis, with seizures, and with a 'sympathetic storm', a hyperreaction of the sympathetic nervous system that causes seizure-like symptoms. Some people with COVID-19 briefly lost consciousness, others had strokes. Even mildly affected patients reported losing their sense of smell. And intensivists wondered whether in some cases, infection depressed the brain stem reflex that senses oxygen starvation. This was another explanation for anecdotal observations that some patients were not gasping for air, despite dangerously low blood oxygen levels.

Discovery of a persistent alcohol-cue memory trace

PhD student Esther Visser and colleagues in the team of Michel van den Oever of the CNCR at VU Amsterdam investigated how alcohol memories are stored in the brain and how this contributes to relapse after prolonged abstinence. Their findings were published in Science Advances.

Esther Visser

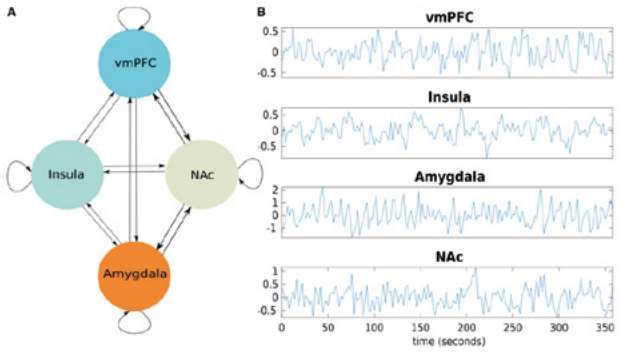
Treatment of alcohol use disorder is hindered by relapse to alcohol drinking, which can occur even after years of abstinence. Relapse can be caused by environmental cues that trigger reactivation of alcohol memories, leading to intense feelings of craving and the urge to resume alcohol consumption. This study investigated in mice how long-term associations between alcohol and environmental cues are encoded in the brain. They found that a small group (~6%) of neurons in the medial prefrontal cortex (mPFC) is highly activated during alcohol consumption in the presence of a cue that signals the availability of alcohol.
Using a genetic tagging technique called viral-TRAP, they were able to express a designer receptor (DREADD) into these activated neurons, allowing subsequent chemogenetic manipulation of their activity. By selectively inhibiting these specific cells, cue-evoked relapse to alcohol seeking after a long abstinence period was substantially reduced. Inhibition of a similar sized different subset of mPFC neurons did not affect relapse. Furthermore, the response appeared to be alcohol specific, since no response was observed in response to sugar after long abstinence. Together, their data revealed that a small subset of neurons in the mPFC encodes an alcohol-cue memory, thereby functioning as a lasting memory trace. The discovery of this alcohol-cue memory trace enhanced our understanding of the fundamental mechanisms of alcohol memory storage in the brain and may be an important lead for development of therapeutic therapy to treat relapse.

Negative mood and anxiety can be modulated by deep brain stimulation for obsessive-compulsive disorder

Researchers of Amsterdam Neuroscience, including Egill Axfjord Fridgeirsson, Guido van Wingen and Damiaan Denys, studied the impact of deep brain stimulation in obsessive-compulsive disorder (OCD) patients and published an article in Brain on the functional connectivity and changes in mood.

Deep brain stimulation (DBS) is an emerging treatment option for patients who do not respond sufficiently to other treatments. For those patients, DBS has a ~60% responder rate. It is shown that DBS of the ventral anterior limb of the internal capsule rapidly improves negative mood and anxiety. To understand these rapid effects, the functional interactions within the affective amygdala circuit was studied. Egill Axfjord Fridgeirsson et al. compared resting state functional MRI data during chronic stimulation versus 1 week of stimulation discontinuation in patients, and obtained two resting state scans from matched healthy volunteers to account for test-retest effects. This data shows them that the improvement in mood and anxiety following DBS was associated with reduced amygdala-insula functional connectivity. Directional connectivity analysis revealed that DBS increased the impact of the ventromedial prefrontal cortex on the amygdala, and decreased the impact of the amygdala on the insula. These results highlight the importance of the amygdala circuit in the pathophysiology of OCD, and suggest a neural systems model through which negative mood and anxiety are modulated by stimulation of the ventral anterior limb of the internal capsule for OCD and possibly other psychiatric disorders.

Figure 1 The causal neural model for the effects of DBS.



(A) A graph model showing the fully connected model with four regions, the vmPFC, insula, amygdala, and NAc. In a fully connected model, each region is reciprocally connected and each region has a self-inhibitory connection. **(B)** Blood oxygen level-dependent time series data from regions of interest from one subject.

Brain, awaa100, https://doi.org/10.1093/brain/awaa100

Uffelmann and Posthuma cross boundaries in the Brainscapes consortium

As part of a University Research Fellowship at the Department of Complex Trait Genetics of Amsterdam Neuroscience, Emil Uffelmann and Danielle Posthuma reviewed resources and methods used by geneticists to point to the most-likely biological mechanism underlying a psychiatric condition. Their review includes a detailed overview of tools and resources of assistance in interpreting GWAS results and is published in Biological Psychiatry. It is the first paper by the Brainscapes

The Brainscape consortium – a Zwaartekracht funding major program under direction of Danielle Posthuma c.s. - uses external data resources on e.g. gene-expression to prioritize a number of genes in their genome-wide association studies (GWAS) results. With newly-developed statistical methods, they can subsequently search for convergent functions among those genes. In their review paper published from this line of research Uffelmann and Posthuma outline several obstacles that need to be overcome in order to make this strategy a winning one. Among them is the relative scarcity of patient data and an overreliance on adult post-mortem tissue in current resources that may not accurately reflect the consequences of genetic disturbances observed in GWASs. They further argue that future resources need to be extended to account for the multi-dimensional nature of neuropsychiatric traits. Moreover, it will necessitate interdisciplinary approaches to solve the ramifications of polygenic-trait architectures. Ultimately, it will be neurobiologists that will need to confirm the results of genetics in-silico analyses in functional follow-up studies. To make this process as efficient and successful as possible, both fields need to actively collaborate in order to capitalize on each other's domain-specific expertise.

Danielle Posthuma and Emil Uffelman

Brigit de Jong and Eva Strijbis launch MS dashboard

How many people with MS have a certain course of the disease? And who is treated with a specific type of medication? These important questions should be answered quick and easy. Thanks to the project value-driven healthcare and the effort of many people the MS Dashboard has been launched. This dashboard helps to determine which care will have an effect on an individual patient.

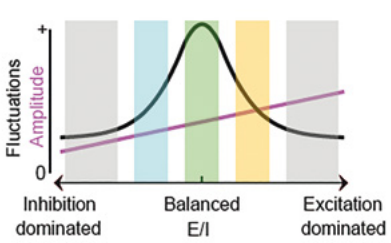
Eva Strijbis

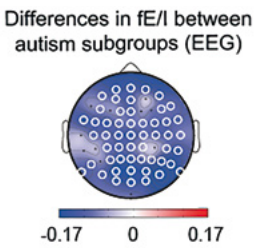
Brigit de Jong

Eva Strijbis: "The MS Dashboard provides us with a better overview of the different types of patient groups we are treating. We can classify them by MS type (relapsing-remitting or progressive), by the use of a specific type of medication, or see how often certain side effects are experienced. This helps us to inform individual patients more accurate, and tailor the medical care to their needs. We can also see how the individual patient is doing over time. We are still working on further development, so that the patient can also view his or her course of the disease in 'MijnDossier' in the future."

From critical brain dynamics to E/I heterogeneity in autism

The group of Klaus Linkenkaer-Hansen, from the department of Integrative Neurophysiology (INFlab) of the CNCR at VU Amsterdam, established a method to estimate excitation/inhibition balance using the theory of critical brain dynamics. By teaming up with the group of Hilgo Bruining from Amsterdam UMC, the method is validated for physiological stratification of autism spectrum disorder.





Computational techniques are increasingly used to translate preclinical concepts to clinical applications in psychiatric disorders. For instance, perturbations to excitation (E) and inhibition (I) balance affecting cognition have been suggested in many disorders but methods to measure E/I ratios in human brain networks have been lacking. To tackle this challenge, the group of Klaus Linkenkaer-Hansen has been long focusing on "criticality" as a strong theory-driven translational framework. The assumption is that a network poised at the critical point exhibits optimal information processing capabilities and that this state requires E/I balance. In Klaus' group, Richard Hardstone has used criticality to develop a method to quantify E/I ratio (fE/I) from neuronal oscillations using their computational model of critical oscillations (CROS). Child Psychiatrist Hilgo Bruining and his team recently joined Amsterdam UMC following intensifying collaboration with the group of Klaus to optimize clinical translation of this solid framework.

Because of the clinical potential, the researchers have filed a patent on the method to protect the IP for commercial use. However, the method is freely available for academic research and collaborating parties are welcome. Amsterdam UMC signed a formal collaboration with Roche to further validate the technology under the supervision of Bruining and Linkenkaer-Hansen.

1.5 million for final phase of Human Brain Project

The European Commission has recently approved the start of the third and final phase of the Human Brain Project. The University of Amsterdam has a leading role within this large, international project, that aims to study the human brain and its diseases with the newest high-tech methods. UvA researchers at the Swammerdam Institute for Life Sciences receive a grant of 1.5 million euros for their contribution to this final phase.

The University of Amsterdam will continue to play a leading role in the Human Brain Project and EBRAINS. The research group Cognitive and Systems Neuroscience (part of the UvA's Swammerdam Institute for Life Sciences), has received a grant of 1.5 million euros for this final phase. For the next three years, the group will contribute to the infrastructure by building a computer model of the cortex and simulating how large amounts of interconnected neurons facilitate cognitive abilities such as perception, recognition and categorization of objects. Amongst other things, the novelty of this work lies in the combination of detailed biophysical modelling of neurons with the performance of high-level cognitive functions that can be achieved at the level of neuronal networks spread out across many brain structures.

The team, including Jorge Mejias, Umberto Olcese, Conrado Bosman, Angelica da Silva Lantyer and Cyriel Pennartz, will also contribute by implementing a smaller model of this system on a chip that mimics the hardware properties and connections of biological neurons (neuromorphic computing). The construction of all models is based on experimental research on how neurons in the cortex code object features and learn from images how to distinguish them from the background. To realize this component of the HBP, the team will integrate supercomputing, simulation and data facilities across Europe, and collaborate in particular with researchers from Germany, Switzerland, Italy, the United Kingdom and Norway.

Largest comparative study provides insights for childhood-onset mental disorders

The worlds' largest comparative study with brain scans of patients with ADHD, ASD and OCD showed subtle, but interesting, differences in subcortical and cortical brain structures. This study is performed by the ENIGMA consortium, a worldwide collaboration that brings together researchers in imaging and genetics to understand brain structure, function, and disease, based on brain imaging and genetic data. Researchers of Amsterdam UMC and Radboudumc published their findings in the American Journal of Psychiatry.

Odile van den Heuvel

With the support of the ENIGMA consortium (abbreviation for Enhancing NeuroImaging and Genetics through Meta-Analysis) brain scans of children and adults from all around the world were compared in large numbers. Using brain scans of 12,198 individuals from 151 cohorts worldwide, the researchers extracted subcortical volumes, cortical thickness, and cortical surface area estimates, using harmonized data processing protocols. This provided the researchers with an enormous amount of data and created an ideal position to investigate overlap and specificity of ADHD, ASD, and OCD. Odile van den Heuvel, professor of neuropsychiatry at Amsterdam UMC who led the analysis, says: "With this first publication we show that worldwide collaboration at this large scale is possible."

The results revealed differing patterns of subcortical and cortical alterations among the disorders across childhood, adolescence, and adulthood. They showed that children and adolescents with ADHD specific have smaller intracranial volume and adults with ASD specific have thicker frontal cortices. There were no OCD specific findings. No brain differences were shared among all three disorders. Overall, the results are robust, but subtle, and they support previous work that emphasize brain differences in the three disorders.

SNAREopathies: new syndrome classification based on mechanism

A position paper by Matthijs Verhage, professor of functional genomics at VU Amsterdam, and his Danish colleague Jacob Sorensen published in Neuron proposes to unify syndromes caused by mutations in eight core components of the synaptic secretion machinery, based on common etiology and mechanism.

Matthijs Verhage

The neuronal SNAREs (soluble NSF attachment protein receptor) and their key regulators together drive synaptic vesicle exocytosis and synaptic transmission as a single, integrated membrane fusion-machine. Human pathogenic mutations are now reported for all eight core components, but patients are diagnosed with very different neurodevelopmental syndromes: children carrying mutations in a single SNAREopathy gene can have >20 different diagnoses, depending on how they entered the health care system, a situation referred to as the diagnostic odyssey for the families/caretakers.

In their position paper Verhage and Sorensen define SNAREopathies and chart the landscape of resultant neurodevelopmental conditions with its complexity in symptoms and disease mechanisms. The authors suggest explanations for the diversity in symptoms by considering (a) partial genetic redundancy, and (b) subtle differences in the cellular impact of mutations among different neurons in the brain. Investigating these suggestions will improve connections between disturbed molecular function of the synaptic secretion machinery and the diverse clinical symptomatology, and ultimately define outcome measures to evaluate future treatments.

Neuroscientists receive funding for frontotemporal dementia and Parkinson research

Neuroscientists from Amsterdam UMC and VU Amsterdam will collaboratively start their research into nerve cells from patients with Parkinson's disease and frontotemporal dementia (FTD). Ultimately, this research supports drug development for FTD and Parkinson's

disease. Recently the Top Sector Life Sciences & Health (Health-Holland) awarded a subsidy for this new research by Yolande Pijnenberg, Wilma van de Berg, and Guus Smit.

Currently, a biobank for stem cells from FTD and Parkinson's patients is being set up. This gives the researchers the opportunity to grow nerve cells from these patients and compare the protein profiles of the cultured nerve cells with the protein profiles of the brain of the deceased patients. By combining clinical, genetic, pathological, and molecular information from the stem cells and brain tissue, the researchers want to unravel common or unique disease processes.

This research project will gain news insight in the clinical, genetic and molecular developments of Parkinson's disease and FTD, which can contribute to the drug development process. Roche will contribute and co-finance in this research project.

Optimization of deep brain stimulation for depression

A team of deep brain stimulation (DBS)-specialists of Amsterdam UMC investigated the optimization of DBS treatment for depression. With a research study led by Guido van Dongen and Luka Liebrand they investigated the relationship between white matter tracts in the brain and DBS treatment response. After published their results in NeuroImage Clinical they strongly advocate for precision psychiatry.

Guido van Wingen

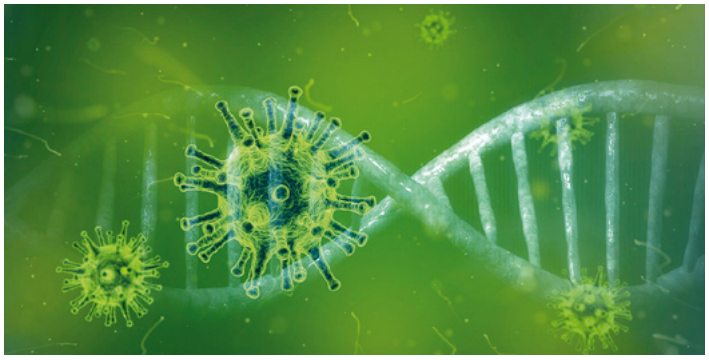
Deep brain stimulation (DBS) is an innovative last-resort treatment for patients suffering from treatment-refractory depression. A team of Amsterdam UMC researchers specialized in DBS, further investigate the role of white matter tracts in the brain of such DBS patients. Allegedly, DBS normalizes pathological network connectivity through the white matter tracts of which those pathological networks consists.

White matter tracts were visualized with a technique called diffusion magnetic resonance tractography. Of special interest were two specific tracts that course through the ventral anterior limb of the internal capsule (vALIC). These tract reconstructions were combined with information of the exact location of the DBS leads, and subsequently associated with treatment response.

Their results suggest that DBS of the vALIC could benefit from targeting white matter bundles. Therefore, the researchers recommend to acquire diffusion magnetic resonance data for each individual patient, advocating precision psychiatry.

Tackling challenges in care during the COVID-19 pandemic for people with dementia

People with dementia have an increased risk of a COVID-19 infection. They also are more likely to develop a severe form of the disease. That has not only to do with their age or the corona-related measures, but also with the genetic factor APOE4. A group of international researchers, led by professor Philip Scheltens from the Alzheimer Center Amsterdam, published a systematic review in the Journal Alzheimer & Dementia.



The impact of the COVID-19 pandemic on healthcare of patients with dementia is enormous. Elderly people with Alzheimer's disease or another form of dementia are faced with lower quality care and extra risks in various institutions. Recent data suggests that people with dementia are more likely to develop a severe COVID-19 infection. Even when factors such as aging and chronic illnesses (e.g. high blood pressure and diabetes) are excluded. It might be that public health measures, such as physical distance or lockdown, have greater adverse effects on the well-being of elderly people with dementia, but there are also biological explanations.

One of the risk factors for Alzheimer's disease is the ApoE4 gene variant. Sixty percent of Alzheimer's patients have this variant, against less than fifteen percent of the general population. A COVID-19 study showed that this factor plays a role in the development of neurological complications in COVID-19. This is because in people with the ApoE4 gene variant the blood-brain barrier functions less. In addition, the gene has a negative influence on the general immune response.

Circadian hormone oscillations preserve a population of neural stem cells in the aging brain

The lab of Carlos Fitzsimons, part of the Brain Plasticity group at the Swammerdam Institute for Life Sciences of the UvA, recently published an article on circadian hormone oscillations and their role in the regulation of neuronal stem cells in the Journal Molecular Psychiatry. The July 2020 edition of this journal is dedicated to advances in depression research, with on the cover the study of Schouten et al.

Carlos Fitzsimons

The focus of the Fitzsimons lab is to identify common mechanisms by which brain insults affect the hippocampus. For this, they focus on a group of insults that modify the proliferation of neural stem cells, resulting in the presence of abnormal neurons and circuit alterations associated with neurodegeneration and cognitive impairment. In their recent publication Fitszimons and colleagues demonstrate how hormone cycles preserve a population of neural stem cells in the aging brain.

With their study Marijn Schouten, Pascal Bielefeld, Paul Lucassen, Carlos Fitzsimons and colleagues show that glucocorticoid hormones oscillations are associated with preserving a specific neural stem/precursor cell population in the dentate gyrus brain area. This suggests a novel mechanism that controls the maintenance of NSPC in the aging brain and presents a possible source of neuroplasticity reserve that could be exploited to sustain hippocampus-dependent cognitive functions throughout life.

COVID-19 Biobank attributes to important reports on causes corona disease

Co-director and professor of neurology Diederik van de Beek and his team responded quickly on the COVID-19 outbreak in the Netherlands. They started the first COVID-19 biobank in the country, by collecting all kinds of samples of COVID-19 patients. They joined the COVID Human Genetic Effort consortium that published two Science reports on common genetic and immunological causes of the life-threatening disease with the support of the Amsterdam UMC COVID-19 Biobank.

Since the COVID Human Genetic Effort consortium have been enrolling thousands of COVID-19 patients to find out whether something in their genetic make-up drives the disparate clinical outcomes the disease produces.

Diederik van de Beek

The researchers genetically analyzed blood samples from more than 650 patients who had been hospitalized for life-threatening pneumonia due to SARS-CoV-2. More than 10 percent of young and healthy people who develop severe COVID-19 have misguided antibodies that attack not the virus, but the immune system itself, new research shows. Another 3.5 percent, at least, carry a specific kind of genetic mutation.

In both groups, the upshot is basically the same: The patients lack type I interferon, a set of 17 proteins crucial for protecting cells and the body from viruses. Whether the proteins have been neutralized by so-called auto-antibodies, or were not produced in sufficient amounts in the first place due to a faulty gene, their missing-in-action appears to be a common theme among a subgroup of COVID-19 sufferers whose disease has thus far been a mystery. Published in two papers in Science, the findings help explain why some people develop a disease much more severe than others.

Yolande Pijnenburg appointed as faculty chair on early onset dementia and as medical director of the Alzheimer Center Amsterdam

As of 1 October 2020, Yolande Pijnenburg is appointed as faculty chair on early onset dementia at Amsterdam UMC, location VUmc. Professor Yolande Pijnenburg will lead the clinical and translational research into dementia, especially at a young age, around the themes: looking for the origin, diagnosis & prognosis, and treatment & prevention. In addition, Pijnenburg will act as medical director of the Alzheimer Center Amsterdam, in close collaboration with the head of clinical research Wiesje van der Flier and director Philip Scheltens.

Yolande Pijnenburg

Over the last decade, Yolande Pijnenburg contributed to the description of so-called early-onset disease phenotypes, and the reappreciation of the behavioural variant of Alzheimer's disease. Pijnenburg has conducted two large descriptive studies on the right temporal variant of Frontotemporal Dementia

(FTD) and the primary progressive aphasias. She sees the acknowledgement of clinical heterogeneity as the essential first step to identify underlying disease mechanisms. Therefore, she collaborated in national and international research that involves biomarker development for (subtypes of) dementia as well as the genetic and pathological background of the disease phenotypes. In the upcoming period, she aims to further establish clinically relevant biomarkers for FTD and its subtypes and in addition will focus on the social cognitive deficits in FTD, ALS and psychiatric disorders. These later group of disorders possibly share a common disease etiology in being moderated by a shared genetic vulnerability in specific neurons and of functional anatomical circuits. In doing so she has already built an international collaborative network that allows for shared data collection and research by integrated teams.

Brain damage in severe COVID-19 infection

The team of Amsterdam UMC pathologist Paul van der Valk shows that COVID-19 is a systemic disease. Inflammatory changes most frequently occurred in the lungs, heart, kidneys, and brain. Their study, published in The Lancet, shows extensive inflammation in the brain, which was most pronounced in the olfactory bulbs and medulla oblongata.

Paul van der Valk

The disease mechanisms are slowly being resolved, clinicians and researchers are only beginning to understand the pathophysiology of COVID-19. The research by Van der Valk and colleagues is based on autopsies carried out on deceased patients suffering SARS-CoV-2. They found that the disrupted immune system of critically ill COVID-19 patients causes damage to all organs, and most notably, the brain. In their study, the virus itself was not found in the brain, but the researchers did find evidence that the immune system of the patients had attacked certain proteins in the brain while fighting SARS-CoV-2.

MS-lesions in most outer layer of the brain visible

Lesions in the cortex, the most outer layer of the brain, have recently become part of the diagnostic criteria for multiple sclerosis (MS), but are notoriously hard to visualize when using conventional MRI-images (sequences). Piet Bouman, PhD candidate at the MS Center Amsterdam, and his colleagues have examined which MRI sequences could best be used in order to visualize cortical MS lesions. Boumans results have been published in the renowned journal Brain.

Piet Bouman

The study shows that cortical MS lesions play a pivotal role in patients' complaints and disease course. Cortical lesions are, however, highly inconspicuous on conventional clinical MRI sequences (T1, T2, FLAIR). In this study published in Brain, Bouman and colleagues found that by the use of the more advanced MRI sequences Double Inversion Recovery (DIR) and Phase-Sensitive Inversion Recovery (PSIR), an increased number of cortical lesions can be visualized.

Royal honor for Philip Scheltens, director Alzheimer Center Amsterdam

Philip Scheltens, director of the Alzheimer Center Amsterdam and professor in cognitive neurology, has been bestowed a royal decoration of Knight in the Order of the Lion of the Netherlands. We congratulate him with this oldest and highest civilian order of chivalry in the Netherlands.

Philip Scheltens

On the 13th of October, Scheltens received the royal decoration out of the hands of Simone Kukenheim, deputy mayor of Amsterdam. Scheltens is an ambassador for Alzheimer's Disease. He has made an essential contribution and has helped to put this disease on the political and social agenda in the Netherlands and overseas. Over the past 20 years, Scheltens has been the driving force behind numerous fundraising initiatives with other parties, such as companies, individuals and foundations.

First study worldwide on discontinuation of antidepressants

How do you reduce the use of antidepressants safely and without major problems? That is a question that concerns many patients and physicians. Amsterdam UMC and Radboudumc in the Netherlands are going to investigate this with a ZonMw grant of 1.5 million euros. The so-called TAPER-AD study with Christiaan Vinkers being the coordinator is the first robust study worldwide to directly compare two tapering methods.

Researcher and psychiatrist Christiaan Vinkers, Amsterdam UMC: “Many patients stop taking their antidepressant at some point. For example, because they have been going well for some time or because they suffer from side effects”. Co-researcher and psychiatrist Eric Ruhé, Radboudumc adds: “Hardly any research has been done on how to discontinue antidepressants best in order to stop. That is actually quite strange when you consider how many people use these medications.”
The researchers are now, in collaboration with – among others – the Dutch patient-organization for depression, the Depression Association, going to look at the best way to taper down. As collaborator in this project dr. Eric Ruhé (Nijmegen) says: “We compare a usual and slower tapering strategy for paroxetine and venlafaxine. These two commonly used antidepressants are the most difficult to taper off. For example, we are investigating whether one way of tapering off causes more discontinuation symptoms than another. But also whether it is more likely that with one of the two tapering strategies the depression will return in the longer term. We also look at effectiveness, quality of life and cost-effectiveness. This knowledge will be of great help to patients, physicians and policymakers.”

The TAPER-AD study uses the infrastructure that the national OPERA study has already built up. OPERA examines who can stop antidepressants and when, while TAPER-AD looks at how to stop. Three other universities (UMC Groningen, UMC Leiden and Erasmus MC) are also involved in TAPER-AD through the collaboration with OPERA.

Consortium receives grant to improve Precision Electroconvulsive therapy for depression

A consortium of depression researchers, led by psychiatrist Annemiek Dols, receives 600,000 euro from the Dutch organization for health research ZonMw. With this ZonMw grant, the clinical scientists analyze and advance electroconvulsive therapy for people suffering from depression. The Precision Electroconvulsive Therapy consortium is a good representation of a large national collaboration with eight different institutes on board.

Brain stimulation with electroconvulsive therapy (ECT) is a safe and effective treatment for depressive episodes, even when psychotherapeutic and psychopharmacological interventions have failed. However, the use of ECT is surprisingly low in the Netherlands. This might be due to (1) limited knowledge on the optimal position in the treatment algorithm, (2) lack of knowledge on cost-effectiveness, (3) fear for side-effects and the outdated representation of ECT. The Precision Electroconvulsive Therapy Consortium wants to fill these knowledge gaps. The ZonMw grant makes it possible to analyze (cost-) effectiveness and side-effects of ECT and compare it to treatment with antidepressants in merged clinical and research cohorts.

Vidi grant for three neuroscience researchers

Christiaan Vinkers, Betty Tijms and Camiel Boon have been awarded a Vidi grant by the Dutch Research Council NWO. NWO has awarded 81 experienced researchers a Vidi grant worth 800,000 euros. The grant enables them to develop their own innovative line of research and set up their own research group in the coming five years.

Christiaan Vinkers: Understanding the impact of childhood trauma in depression

Christiaan Vinkers

Betty Tijms

Camiel Boon

Many people experience childhood trauma which increase the risk for psychiatric disorders such as depression. But can people recover from childhood trauma? This project tries to understand the long-lasting and severe impact of childhood trauma and test whether a ‘reset’ of the stress system can help to treat depression related to childhood trauma.

Betty Tijms: Strong brain connections for resilience to dementia
Brain functioning relies on the connections between brain areas. Alzheimer’s disease disrupts brain connectivity and causes dementia. However, individuals who have strong brain connections show slower disease progression. The researchers will investigate which biological processes contribute to strong brain connectivity, in order to find novel ways to delay Alzheimer’s disease.

Camiel Boon: Developing cutting-edge treatments to combat early hereditary blindness
X-linked juvenile retinoschisis (XLRS) is a relatively common hereditary eye disease, for which there is no treatment. XLRS causes severe vision loss or even blindness in childhood. I will develop a cure for XLRS in experimental models that mimic the disease, based on patient-specific stem cells and an animal model.

Veni grant for three neuroscience researchers

Jeanne Savage, Anita van Loenhoud, and Aishu Parthasarathy have been awarded a Veni grant by the Dutch Research Council (NWO). The Veni grant is worth up to 250,000 euros and this year 161 highly promising young scientists received this grant by NWO. The grant provides the laureates with the opportunity to further elaborate their own ideas during a period of three years.

Jeanne Savage: Multiple genetic pathways to alcohol misuse
Alcohol misuse is a highly heritable behaviour with enormous global health burden and societal costs, yet the specific genes involved remain elusive to detect. This study aims to improve gene identification by considering the complexity of alcohol misuse and examining the possibility of multiple genetic pathways in its development.

Anita van Loenhoud: The brain's reserve capacity in Alzheimer's disease
Why are some people with Alzheimer's disease better protected against memory problems than others? This project examines the "reserve capacity" of the brain, by studying differences between patients in their course of symptoms and brain changes. This work will contribute to better prognostic tools and novel disease-modifying treatments for Alzheimer's.

Aishu Parthasarathy: The integrated neural code of action selection and action-outcome valence in the basal ganglia
We naturally pursue rewarding experiences actively, but choose to be passive in order to avoid aversive stimuli (not being proactive). This proposal aims to identify how and why our brain biases our action choice differently in rewarding and aversive situations, a phenomenon that is also highly relevant in psychiatric disorders.


Jeanne Savage


Anita van Loenhoud


Aishu Parthasarathy

Large consortium multiple sclerosis 'Don't be late' awarded with grant

A group of MS researchers and supportive organizations, led by Amsterdam UMC neuroscientist Hanneke Hulst, has been awarded funding within the second round of the Dutch Research Agenda (NWA), called Research along Routes by Consortia (NWA-ORC). Their mission is to postpone cognitive decline and prevent unemployment in patients with multiple sclerosis (MS).

Hanneke Hulst

The Dutch Research Council supports the work of this interdisciplinary consortium with the name 'Don't be late' that will bring together scientific and societal breakthroughs within reach. Hanneke Hulst and her colleagues are awarded 1,6 million euros. The consortium wants to postponing cognitive decline and preventing early unemployment. Cognitive decline is one of the symptoms of MS, affecting up to 70% of the (young) people with MS. When patients with MS report cognitive and work-related problems, these problems are often too advanced for treatment. Intervening sooner rather than later is crucial, which requires a paradigm shift from symptom management towards prevention of symptoms. By focusing on prevention, quality of life and participation in society will be enhanced.

NWA Grant for integrating human principles in AI

A collaborative consortium of Dutch researchers and partners from the private and public sector will focus on bringing human principles into AI solutions to integrate smart machines in society. They received a grant of 3,5 million euros for their research proposal 'Perceptive acting under uncertainty: safety solutions for autonomous systems'. Prof. Sander Bohté, professor by special appointment at the UvA's Swammerdam Institute for Life Sciences (SILS-UvA) and senior researcher at the Centrum Wiskunde en Informatica (CWI), will take the lead in the research project.

Sander Bohté: "I am really excited about the possibilities the NWA-ORC grant will offer our consortium. It allows us to develop insights from neuroscience and psychology to put society back "in-the-lead" in the rapid developments surrounding AI and smart vehicles. We focus on answering the question how humans, in particular "brains", deal with uncertainty in complex situations like traffic, and transfer these insights into both AI algorithms that are more predictable, and recommendations for the associated

regulatory control frameworks that incentivizes such behavior. This human-centered approach will allow society to take back control: we strongly believe that societal needs should drive these far-reaching AI developments rather than the other way around."

From SILS-UvA, Dr Jorge Mejias and Prof. Cyriel Pennartz are also involved in the project. Their contribution will focus on reinforcing the connection between neuroscience and AI, in order to develop brain-inspired AI algorithms for safe mobility. With their expertise in experimental, theoretical and computational neuroscience, they will analyse existing neurophysiological and neuroanatomical data to develop computational models of realistic brain circuits involved in perception under uncertainty. A key element is to build models that can draw inferences from sensory inputs and can represent objects and environments causing these inputs to arise.

ERC Consolidator Grants for Matthijs Brouwer and Martijn van den Heuvel

The European Research Council (ERC) has awarded the Consolidator Grants to neurologist Matthijs Brouwer and computational neuroscientist Martijn van den Heuvel. The prestigious grants are awarded to individual researchers and amount to around 2 million euros per project. With the grant Brouwer wants to improve the cause-specific diagnosis of encephalitis using innovative diagnostic methods. Whereas Van den Heuvel will study patterns of brain connectivity towards a common mechanism of mental conditions and prediction connectomics.

Matthijs Brouwer – Improving prognosis by using innovative methods to diagnose causes of encephalitis


Matthijs Brouwer

Severe inflammation of the brain

Encephalitis is a severe inflammation of the brain that can be caused by bacteria, viruses, fungi and parasites, as well as by overactivity of the immune system. In half of the people with encephalitis, however, the cause remains unclear, and it is therefore difficult for doctors to choose the optimal treatment. One in six patients with encephalitis dies, which is partly due to the treatment delay caused by the uncertainty on the cause of the problem.

Torturing cerebrospinal fluid on the cause of encephalitis until it will confess

With the research project called IPACE: 'Improving Prognosis by Using Innovative Methods to Diagnose Causes of Encephalitis' Brouwer wants to identify the cause of encephalitis for early initiation of therapy. Brouwer will be searching for new causes of encephalitis in a large group of patients. He will use innovative techniques to study cerebrospinal fluid in order to identify previously unknown viruses and other pathogens. By looking at patterns of gene expression (RNA), lipids, metabolites and proteins in cerebrospinal fluid, he wants to find a fingerprint of each cause of encephalitis, allowing for the cause to be determined within a few hours. This will enable fast and targeted treatment and thereby improve the prognosis of patients with encephalitis. Brouwer aims to discover novel causes of infectious and autoimmune encephalitis, and provide insights in its pathophysiology.

Martijn van den Heuvel - Connecting cross-condition patterns of brain connectivity towards a common mechanism of mental conditions and prediction connectomics


Martijn van den Heuvel

Maps of the human brain

Van den Heuvel can be seen as one of the pioneers in the field of 'connectomics', the arena that studies the human brain from a network perspective. With his research Van den Heuvel wants to build the most detailed network of the human connectome possible. This 'google maps' of the human brain will greatly help to investigate the relationship between how our brain is wired and the rich spectrum of cognitive behavior and function we display. By studying the maps of the human brain in detail, Van den Heuvel wants to see where there may be vulnerabilities in our brains. The techniques used to study and compare these maps are still in the early phase of development. With this ERC grant Van den Heuvel will improve and simplify those analysis techniques.

Risk genes and risk connections

An important question that Van den Heuvel wants to address with his study is whether there is a connection with genetics. More and more genetic research show that different risk genes are involved in brain disorders. People may have a 'predisposition' to develop Alzheimer's disease or insomnia. With the ERC grant Van den Heuvel wants to answer the following questions: how do these genetic vulnerabilities relate to connectivity vulnerabilities? Are certain connections more susceptible to disruption, and is this related to genetic vulnerabilities?

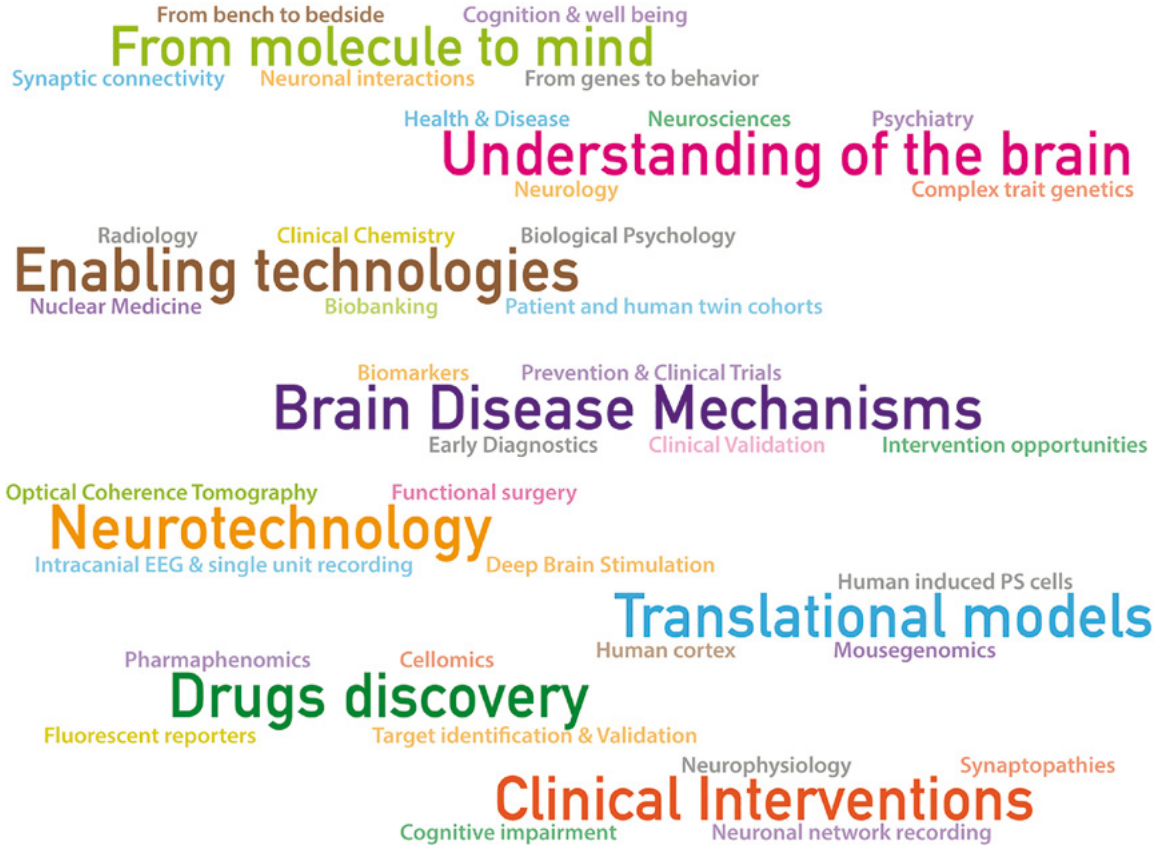
People with a mental health disorder suffer more from the COVID-19 pandemic

People who have had a mental health disorder, suffered more from the COVID-19 pandemic compared to people without a mental health disorder. They reported more symptoms like depression, anxiety and loneliness. However, the severity of the symptoms did not increase compared to the period before the COVID-19 pandemic.

Brenda Penninx

The Amsterdam UMC investigated the impact of the COVID-19 pandemic on the mental health of 1,500 people with an existing mental health disorder in three psychiatry case-control cohorts. Kuan-Yu Pan (research associate at Amsterdam UMC) and Brenda Penninx (professor of Psychiatric Epidemiology at Amsterdam UMC) were part of the research team. Their study showed that people with pre-existing mental health disorders experienced a higher impact of the corona pandemic on their mental health. They reported more fear of an infection and poorer ability to cope with this stressful event. On average the researchers did not find a change in the severity of depression, anxiety or loneliness symptoms of people with a mental health disorder, when they compared symptoms before and during the COVID-19 pandemic. The symptoms of people with severe mental health disorders even seemed to decline.

Amsterdam Neuroscience



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