



THE NETHERLANDS BRAIN INITIATIVE

MANIFESTO

ACHIEVING
GREATER
IMPACT
TOGETHER



Foreword

You have before you the manifesto of Nationaal Plan Hoofdzaken ('The Netherlands Brain Initiative'). The Netherlands Brain Initiative is an initiative of the Brain Foundation Netherlands, MIND, ZonMw, NWO and Health~Holland and has been developed with experts from various disciplines. We are advocating a national knowledge and innovation programme on brain and mental disorders with a duration of at least 10 years with structural funding. A programme without dividing lines, where connections and cross-fertilisation take place between disciplines such as psychiatry and neurology. The focus is on innovation for patients, so we can achieve greater impact in the years to come.

For many years, I have enjoyed working on the development and improvement of health research policy in the Netherlands. I have seen many things change and come together, but this manifesto comes top of the list, as it is truly unique for several reasons. First, because we are moving beyond the separation of mind and body and opting for a holistic approach. This may seem obvious, but in practice it is still difficult. What also sets this initiative apart is that we have brought together all the parties in mental health care, the neurosciences, and the social sciences and humanities to work together. Where previously these parties worked independently, the aim now is to share knowledge and set up projects together. This is the only way to achieve effective innovation for patients.

It is remarkable to see how committed everyone is to this cause. We have only been able to achieve this thanks to the great and intrinsic drive of all participants and initiators. Together, we have joined forces, allowing us to achieve additional research and innovation to combat neurological and mental suffering. I would like to thank the initiators and the experts, including those with personal experience, involved in this manifesto. We have had many interesting conversations and discussions. All aimed at achieving the best possible outcome.

I see this manifesto as a trend breaker and hope that it will enable us to reduce the expected growth in the burden of disease in this area. I sincerely hope this manifesto inspires you and, above all, encourages you to take action, so the inspiring words in this document are transformed into highly relevant research and innovation within healthcare. Together, we are committed to the patient of today and tomorrow.

Henk Smid, chair of the Netherlands Brain Initiative Steering Committee

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Summary

THE NETHERLANDS

BRAIN INITIATIVE:

tackling brain and mental disorders together

A quarter of the people in the Netherlands suffer from brain and/or mental disorders. The limited options for intervention lead to problems for the individuals, their environment and society. Every year, 20% of the people that die in the Netherlands die from a serious brain disorder. Living with such a condition takes a heavy toll on people. Work, education and social contacts are disrupted. The healthcare costs are also huge: over EUR 25 billion a year. This is more than a quarter of the total health care costs in the Netherlands, and this figure is expected to rise sharply.

To solve this problem, we need more knowledge. About how our brain works, what can go wrong and how the condition can be improved. But also about social aspects. After all, our mental functions and our brain are irreplaceable, and its functioning is complex and all-encompassing. We know a lot about it, but we still know far too little. It is a relatively young and largely unexplored field, and there is still too little collaboration. Not only between different science disciplines, but also between science and practice. Investment is short-term and fragmented. And innovations do not always reach patients in time.

Together with patients and their loved ones, researchers, healthcare professionals, knowledge institutions, companies, and social and governmental organisations, we have the ambition to enable people with brain and/or mental disorders to live five years longer in good health by 2040. To achieve this, we are working on a national knowledge and innovation programme on brain and mental disorders based on three opportunities. This programme brings together knowledge and data from psychiatry, psychology, neurology and neuroscience, and brings better solutions for patients into practice faster. These three opportunities are:

OPPORTUNITY 1



Faster implementation of solutions for patients. This means:

- Involving patients and their families as collaborators in all phases, from scientific research to care practice;
- Accelerating the knowledge cycle by fostering entrepreneurship.

OPPORTUNITY 2



Combining knowledge on disorders. Specifically, this means:

- investing in research into cross-disorder similarities in symptoms, causes, underlying mechanisms and solutions;
- developing new techniques for precision medicine and personalised lifestyle interventions.

OPPORTUNITY 3



Better sharing of knowledge and data by:

- encouraging collaboration and sharing of knowledge, techniques and data at all levels and between all disciplines;
- organising networking and interdisciplinary communication.

We are thus building an infrastructure that will deliver solutions to prevent brain and/or mental disorders, improve treatments or enable people to live better with a brain-related disorder. With the needs of the patient at the centre. This is how we make a difference for millions of Dutch people.

Join us in making brain and mental health the main issue!

Initiators Brain Foundation Netherlands, MIND, ZonMw, NWO and Health~Holland

Make brain and mental disorders a top priority

The Netherlands Brain Initiative is a broad movement aiming to create solutions for people with brain and/or mental disorders. This is urgently needed because these disorders affect one in four Dutch people and cause major problems for patients, their families and society as a whole. Together, we are working towards brain health and mental health in the broadest sense.

Every patient, every brain and every situation is unique. This makes brain and mental disorders complex diseases. Many different genes, sex and gender variations and a range of social and physical conditions contribute to their onset and expression. That is why the Netherlands Brain Initiative is opting for a radical transformation. We are no longer using specific disorders as our starting point but are focusing on the patient's unique and always complex situation instead. This requires a holistic view, looking at parallels between causes, underlying mechanisms, treatment of conditions and strengthening people's ability to recover. This is how we can make a real difference.

WORD CHOICE

The Netherlands Brain Initiative is committed to all disorders related to the brain and wants to give full scope to the different perspectives on biological, psychological and social issues within the initiative (and future programme). As it is difficult to summarise this in one word, we have chosen terms such as brain and/or mental disorders and brain-related disorders. We would like to emphasise that these should be interpreted broadly and are intended to be all-encompassing.



People with brain-related disorders are waiting for breakthroughs in their treatment. Thanks to new techniques and developments, some of these breakthroughs are within reach. But they will only be achieved if we take big steps now by investing heavily in a holistic approach. If we want to keep care accessible, high-quality and affordable, we need to set a transformation into motion.

The Netherlands Brain Initiative is a movement with a unique plan. We are abandoning the traditional division between psychiatry, psychology, neurology and neuroscience and focusing on the connection. Not only between various disciplines, but also between all phases of the knowledge cycle. This is how knowledge will pay off. We are also stimulating and using activities in health-care practice, policy, education and research. Patients are given an important voice and role in this process.

The Netherlands Brain Initiative advocates a national knowledge and innovation programme on brain and mental disorders with structural funding. A programme without dividing lines, with connections and cross-fertilisation between disciplines and domains. We do not lose sight of the added value of unique areas of expertise. We are making new connections, always focusing on innovation for patients. We want to accelerate by ending fragmentation. We will not only continue to identify and analyse all the pieces of the puzzle, but above all, we will put the different pieces in their right place.

This manifesto will explain why this is so important and what opportunities we have identified. We start by explaining the complexity of brain and mental disorders. Then we will discuss the research that is needed to bring us closer to finding solutions. Finally, we look at the three opportunities:

1. Faster implementation of solutions for patients.
2. Combining knowledge on disorders.
3. Better sharing of knowledge and data.

Our goal is to better understand, prevent, treat and, if possible, cure brain and mental disorders.

Patients and their families are crying out for help. And they want help that matters. We want to join them in responding to this cry for help. This is the momentum to put the pieces of the puzzle in their right place. Join us in tackling brain and mental disorders!

Brain and mental disorders are **a top priority**

The brain is essential to our daily functioning

Our brain is not just an organ with cells and various physiological processes. It is also the pilot of our body, the repository of our memory, the engine behind our thinking and the switchboard through which we relate to the world around us. Our brain sets the stage for our mental functioning. It is also indispensable, irreplaceable, almost impossible to repair, and its workings are more complex and extensive than that of any other organ. Our brain is literally the nerve centre of our body. Yet it is also the part of the body that we know the least about. This has far-reaching consequences.

One in four Dutch people have a brain-related disorder

In a complex system such as the brain, things can go wrong for a variety of reasons. A quarter of all Dutch people suffer from one or more brain and/or mental disorders. These often cause a variety of serious problems for themselves and their relatives (family, friends, loved ones). The spectrum of brain disorders is broad and complex. It ranges from well-known disorders such as dementia, epilepsy and migraine to a variety of rarer ones. The latter often have a genetic background and manifest themselves in early childhood. Exactly how the brain relates to mental suffering is unknown and difficult to study. But the hypothesis that brain processes may be contextually relevant to mental suffering is something we cannot avoid. Therefore, in the Netherlands Brain Initiative, we also include mental suffering under the term brain-related disorders.

Often complex causes

Heredity and a wide range of social and/or physical conditions often play a role in the development of brain and mental disorders. The same disorders can also manifest themselves in very different ways. There are also gender and sex differences, which can be further explored and to which care can be tailored accordingly.

'I will never be my old self again, so I try to embrace the new me as much as possible, including its qualities and limitations.'

Woman after
suffering from meningitis

What links these disorders is that processes in the brain play a role. This requires good research, for example to see if changes in context can help alleviate the suffering of people with brain and/or mental disorders. It is important to distinguish between disorders on the one hand and variation between people on the other. Variation in our brains sets the stage for variation in who we are. For example, the level of intelligence we have and the extent to which someone is more vulnerable to stress or more resilient. In this respect, mild intellectual disability or giftedness, for example, is a matter of variation rather than a disorder. Of course, everyone may need care or support at some point in their lives.

DISORDERS

Common disorders in which the brain may play a role include mental disorders (such as anxiety, eating disorders, depression and addiction), neurodegenerative disorders (such as dementia, Parkinson's and ALS), non-congenital brain injuries (such as stroke or brain damage after an accident), developmental disorders (such as ADHD and autism) and other disorders (such as epilepsy, cerebral palsy and a brain tumour).

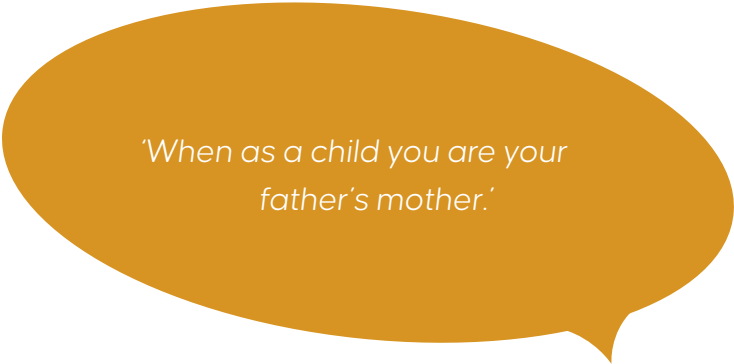


Early onset, lifelong impact

Many disorders involving the brain develop early in life and can cause lifelong problems. Examples include migraine, anxiety disorders, epilepsy, multiple sclerosis or more rare disorders. The same applies, of course, to brain damage caused at birth or by an accident at an early age. The number of years people live with the consequences can be high. Moreover, people often have multiple disorders, for example Parkinson's and depression. It can also be harder for people with brain and/or mental disorders to live a healthy life, which reduces their life expectancy.



Figure 1: A number of brain and mental disorders categorized according to the life stage in which, **relatively** speaking, they most commonly occur. The overview is not exhaustive and is for illustrative purposes only. Data are not available for all disorders. These are data from the Netherlands. Several sources were consulted.



*'When as a child you are your
father's mother.'*

Daughter of a father who is mentally ill

The impact is huge

Brain and mental disorders can affect motor and thinking skills, as well as a person's unique qualities. Personality, humour and interests can be altered by brain and mental disorders. Symptoms such as mistrust, addiction, self-harm, personality change, apathy and impulsiveness can make it difficult to form or maintain good relationships. The burden and suffering for both patients and their families is often considerable. Not surprisingly, the problems of children of parents with brain and/or mental disorders are also receiving increasing attention.

Major societal impact as well

The burden on society is also considerable. This is mainly due to the high costs of extensive care and support and the loss of work productivity of patients and informal carers. Care costs alone currently amount to EUR 25 billion a year. Work absenteeism is also high. For example, mental disorders such as burnout, depression and post-traumatic stress disorder have been the most commonly reported occupational illnesses in recent years. In addition, 60% of people do not return to work within two years of a brain injury.

Doing nothing is not an option

The National Institute for Public Health and the Environment (RIVM) expects the number of Dutch people with brain and/or mental disorders and their disease burden to skyrocket in the coming years. In 2040, for example, the burden of dementia will be more than 2.5 times higher than today, and the burden of Parkinson's disease will double. The burden of disease for people with mood and anxiety disorders will remain high. By 2040, mental disorders will be in the top three diagnosis groups causing the greatest burden of disease. The current COVID-19 pandemic has certainly not helped these figures.



THE PROBLEMS ARE HUGE

- One in four people have a brain-related disorder.
- Nearly one in five deaths in the Netherlands are due to brain and/or mental disorders.
- Brain and/or mental disorders have the highest healthcare costs: over EUR 25 billion per year in the Netherlands; more than a quarter of all healthcare costs.
- Brain and/or mental disorders prevent many people from participating in society.
- Mental disorders are the most frequently reported occupational diseases. Approximately 60% of people cannot return to work within two years after a brain injury.
- Brain and/or mental disorders require a high level of commitment from informal carers.
- The National Institute for Health and Environment (RIVM) expects the number of Dutch people with brain and/or mental disorders and their burden of disease to skyrocket.
- COVID-19 infection increases the risk of both psychiatric and neurological disorders.
- People with mental disorders are at higher risk of developing other mental disorders and/or somatic disorders. This increases the impact on wellbeing and society.

Too few prospects for patients and their families

Unfortunately, our ability to prevent and treat, let alone cure, brain and mental disorders is still very limited. Whether common or rare, we still do not know the cause of many brain and/or mental disorders. Although we have made progress in pharmacological, psychotherapeutic, surgical and behavioural treatments, a large number of disorders remain unexplained and often incurable. Brain and/or mental illness has a profound impact on the lives of patients and their families. Personal and social recovery is still a long way off for many patients. This can and must be improved.

'Just because you don't notice anything wrong with me doesn't mean that everything is okay.'

Woman after stroke

Joining forces with the patients of today and tomorrow

Joining forces with the patients of today and tomorrow and their families will enable us to invest much more in implementing promising solutions and ensuring that practitioners and innovative companies act on them. These are often developments that can help someone learn to cope better with a condition, provide personalised treatment or manage symptoms and improve the ability to recover so patients can participate in society again. This approach leads to fewer symptoms, more control and greater participation!

Joining forces with the patients of today and tomorrow and their families will enable us to use all kinds of new knowledge and techniques to finally develop real solutions. Our goal is to gain a better understanding of the causes of these disorders and find ways to address them. We are committed to advancing brain health and mental health. We will, must and can do much more to effectively cure and – even better – prevent brain and mental disorders. Now is the time to commit to these objectives.

'With this innovative approach, we can combat fragmentation and work towards a more common basis for brain research.'

Prof Dr Jeroen Geurts,
chair of the Board of ZonMw

Research on brain and mental disorders is a top priority

Collaborative and creative thinking in a long-term research programme

Progress requires courage and creativity, with room to explore ground-breaking ideas. By joining forces, we can better understand, prevent, treat and possibly cure disorders. The combined efforts of patients, their families, practitioners, scientists and companies are vital. The Netherlands Brain Initiative aims to look beyond traditional boundaries, encourage outside-the-box thinking, create cohesion and collaborate more often and more effectively. All this should take place within a **long-term** national knowledge and innovation programme that recognises the importance of inclusiveness, diversity and gender.

ABUSE AND NEGLECT

As a group, people who were abused and neglected as children have a subtle reduction in white matter volume in different areas of the brain. There is evidence of abnormal development at the molecular level, possibly in areas involved in processing emotion and reward. This could possibly explain why these people are more likely to become addicted to drugs.



More understanding needed

We have only begun to understand how the brain works in the last 50 years. Much is still a mystery. Especially when it comes to mental suffering. The more we learn, the clearer it becomes how incredibly complex and ingenious our brain actually is. Many hypotheses remain untested.

To effectively address brain and mental disorders, research is needed to test these hypotheses. Much more needs to be understood about the brain, including the interplay between biological processes, personal vulnerabilities and environmental factors. The link between biological processes and behaviour is still misunderstood and too often studied and treated in isolation.

Building on our strengths

The Netherlands has a good basis for strengthening brain-related research. In addition to the Netherlands Institute for Neuroscience, our universities and medical centres have combined brain-related research in institutes or programmes. We have a great deal of healthcare expertise, such as rehabilitation medicine, paediatrics and geriatrics, as well as psychotherapy, psychology and psychiatry. The Netherlands Brain Bank is internationally renowned, and other biobanks, patient registers and the many cohorts in the Netherlands also offer the potential to gain more knowledge about people with brain and/or mental disorders. To make this possible, however, we must decide to make brain-related research a top priority!



HERSENBANK VERSTEVIGEN

The Netherlands Brain Bank collects brain material from people (both healthy and people with disorders, and from foetuses and adults) who have donated their brain after death for worldwide scientific research. The Netherlands Brain Bank has been an international leader for many years. Post-mortem examinations often reveal that the diagnosis made during life was not correct. In addition, abnormalities often turn out to be caused by various brain-related diseases. By making brain tissue available to researchers, the Netherlands Brain Bank promotes the understanding of disease processes and thus the development of new therapies for brain-related disorders. Current capacity limits the Netherlands Brain Bank to a maximum of 150 post-mortem studies per year. The Brain Bank could play a much more important role in the Netherlands by expanding its capacity and initiating a brain donation programme in important Dutch research cohorts of people with brain and/or mental disorders. Such investments will lead to more humane brain research and are essential for the transition to animal-free innovation.

In recent years, patients and their families have become much more involved in research and their experience is increasingly being used. Not as 'target groups' or 'objects of suffering', but as drivers and active partners in scientific research. As instigators of problems that need solving, as critical thinkers about which research should be prioritised and funded, but also as participants in the design and implementation of research. The Netherlands Brain Initiative wants to make intensive use of this experience and further stimulate patient participation at all levels.

New technologies need to be applied

New discoveries are increasingly helping us, sometimes literally, to understand the complex systems in our brain. This began with the introduction of the CT scan in 1971, followed a decade later by the MRI. We are now on the verge of studying the brain with techniques such as optogenetics and chemogenetics. Indeed, we can do so much more these days. For example, we can create mini-brains from a skin biopsy of patients and determine which medication is suitable for specific patients. In genetics, CRISPR-Cas has recently made it possible to precisely correct the code of life. These new possibilities need to be applied and, at the same time, ethically assessed and supported in a broad collaborative framework. We can learn from each other not only within the field of brain-related work, but also outside it. For example, CRISPR-Cas technology has already led to positive results with disorders in other areas.



'As a patient organisation, we want to work with doctors and researchers. We are intermediaries for knowledge exchange, for recruitment of research populations and for sharing knowledge from research results.'

Patient survey the Netherlands Brain Initiative



MINI-BRAIN FOR RESEARCH

Researchers are increasingly successful in growing mini-brains from random human cells, complete with nerve cells and blood vessels. These mini-brains make it much easier to study the development of the human brain than in laboratory animals. The mini-brains have already provided new insights into a number of disorders, including autism, microcephaly and Kleeftstra syndrome. Researchers also see possibilities for many other inherited disorders, such as epilepsy, spinocerebellar ataxia, Down syndrome and inherited forms of dementia. There may also be opportunities for problems such as susceptibility to psychosis.

Seizing today's opportunities

At a societal level, there is still an urgent need for social science research into the interrelated mechanisms of prejudice, stigma and exclusion. In the behavioural sciences, new research methods are enabling us to identify aspects of patients' experiential aspects better than ever before. Supercomputers can combine and analyse these huge amounts of data, allowing us to establish new connections that better reflect the interplay between personal, biological, behavioural and environmental factors. The possibilities for developing new solutions and healthcare innovations for brain and/or mental disorders are numerous. But we must seize these opportunities.

Towards personalised medicine and

This will allow us to increasingly determine which treatment works for whom and in combination with what. With personalised medicine, we can identify a patient's highly individual characteristics and study how they relate, for example, to the genetic code, the expression of proteins or all sorts of behavioural traits. This allows us to tailor treatments much more closely to patients' needs and requirements. These possibilities are already being used here and there in medicine, but not yet or rarely for brain and mental disorders. We still have a lot of catching up to do, but in the short term we can significantly improve care. With tailored treatments for the right patient, at the right time, stage and dose.

... lifestyle interventions

At the same time, by combining data from a large number of people, we can actually provide broad prevention advice, such as lifestyle interventions, that are important in preventing brain and/or mental disorders. This includes not only the familiar things such as a healthy diet, not smoking, not drinking alcohol, getting enough sleep and regular exercise, but also the importance of continuing to challenge the brain and the role of the environment. There is a need for more tailored prevention that takes into account people's social and physical environments.

Everyone benefits

Patients and their families are not the only ones who will benefit from investing in comprehensive research into brain and mental disorders. New drugs, treatments, research equipment, medical technology, devices and computer technologies offer opportunities for start-ups and existing companies. Universities, UMCs and research institutes will be able to collaborate across sectors, and healthcare providers will have up-to-date options to help their patients. In addition, patient organisations will have the latest information for their supporters, which they can use to reinforce developments such as 'shared decision-making' and self-management.



MS SHERPA PREDICTS MS DEVELOPMENT

What makes living with multiple sclerosis (MS) particularly difficult is the unpredictable nature of the disease. MS Sherpa is a solution for and by people with MS. Using an app and an intelligent computer program, it calculates how MS will behave and develop for each person. Because the software can learn, it is possible to recognise personal patterns and, on that basis, be able to say more about the course of the disease. This makes personalised therapy truly possible. This form of artificial intelligence is also used, for example, to detect relapses in people with depression. More examples are expected in the future.

Three opportunities

In this chapter, we describe three opportunities that will allow us to make important advances in research on brain and mental disorders, brain health and mental health through a national knowledge and innovation programme. These opportunities have emerged from discussions with patients, family members, healthcare professionals and researchers.



MAKE BRAIN AND MENTAL HEALTH A TOP PRIORITY!

People with brain and/or mental disorders will live five years longer in good health by 2040.

OPPORTUNITY 1 FASTER IMPLEMENTATION OF SOLUTIONS FOR PATIENTS

- Involving patients and their families as collaborators in all phases, from scientific research to care practice;
- Accelerating the knowledge cycle by fostering entrepreneurship.

OPPORTUNITY 2 COMBINING KNOWLEDGE ON DISORDERS

- Investing in research into cross-disorder similarities in symptoms, causes, underlying mechanisms and solutions;
- Developing new techniques for precision medicine and personalised lifestyle interventions.

OPPORTUNITY 3 BETTER SHARING OF KNOWLEDGE AND DATA

- Encouraging collaboration and sharing of knowledge, techniques and data at all levels and between all disciplines;
- Organising networking and interdisciplinary communication.

OPPORTUNITY 1

Faster implementation of solutions for patients

Faster from knowledge to patient solutions

The journey from knowledge to a solution for the patient is long and complex. Consider the pathway from basic scientific research in the laboratory to treatment in the consulting room, or the development of effective devices by start-ups or established companies. There is constant movement between all the stages and actors in the cycle. There are many players, many intermediate stops, many ups and downs. This must be done better and faster!

Identifying opportunities together

A good map of where we are, where there are promising untapped opportunities and where we can accelerate is therefore important. This includes understanding where we can innovate with today's technologies. All of this requires a good grasp of the big picture. It allows us to visualise where the pieces of the puzzle fit together and what we need to complete it.

PARKINSONNET

Caring for people with Parkinson's disease involves many disciplines and healthcare providers. This makes the approach complex. Getting all the healthcare professionals involved to work together and share knowledge provides Parkinson's patients with support in self-management and access to the best care. This leads to better use of guidelines by healthcare providers, fewer treatment sessions and fewer complications. Studies also show that ParkinsonNet reduces healthcare costs.



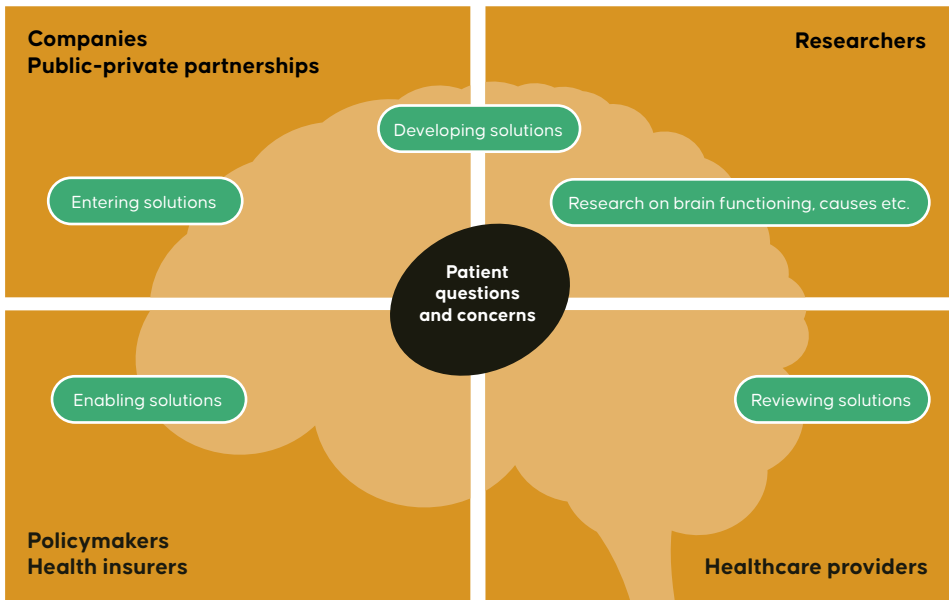


Figure 2: Making knowledge pay off through (better) collaboration within and between all stages of the knowledge cycle.

Effective implementation

The step from collecting and weighing scientific, practical and experiential knowledge into applicable knowledge that can actually be used by the carer, patient or relative requires new effective implementation strategies. Do we really want to force a breakthrough from which we can benefit? Then researchers, practitioners and relevant companies, together with patients and relatives, need to invest more in effective implementation. This can be done, for example, by setting up large regional practice projects such as ParkinsonNet. Such large-scale networks bring together researchers, patients, relatives and practitioners under one roof, thereby promoting the translation of knowledge. Much more than in the past, we will need to involve patients and their families. By increasing their opportunities to participate, they will feel more empowered and will be able to contribute to decisions about investments in the implementation of promising ideas.

Major challenge also for companies, insurers, politicians and funders

We need better links not only within science and with patient organisations, but also between science, patient organisations, industry, insurers, the social sector, politicians and funders. New technologies offer opportunities for start-ups or existing companies. This needs to be facilitated.



DEEP BRAIN STIMULATION

Deep brain stimulation (DBS) is a treatment that uses electrodes placed in the brain to deliver electrical signals. This suppresses specific symptoms, reducing or eliminating them. DBS is currently used in the Netherlands for Parkinson's disease, epilepsy and obsessive-compulsive disorder. Research into its use in depression and Alzheimer's disease is ongoing.

Rewarding inspiration and creativity

We must also learn to think much more outside the box, tap into our creativity and inspire each other across boundaries. This means not only funding existing top research teams, but also providing opportunities for new, refreshing ideas. A clear choice for brain-related research at every university, UMC and research institute helps to build and strengthen the Dutch brain and mental health research infrastructure. It is important to involve companies and other developers in research at an early stage. This way, the knowledge and the products generated can be 'marketed' and more new treatments and techniques will become available to patients and their families sooner.



NANOTECHNOLOGY

The blood-brain barrier not only stops harmful substances, but it also prevents important substances from doing their job in the brain. Substances that could be used in diagnosis or treatment. Nanotechnology offers the possibility of getting drugs through the blood-brain barrier to the right place.

'Nothing About Us Without Us'

Programme Alliance UN Convention on Disability

Leadership and coordination from an up-to-date knowledge agenda

The above highlights the importance of a comprehensive, joint knowledge agenda developed by patients, families, researchers, practitioners, funders and other experts such as ethicists. Establishing and regularly updating such an agenda not only provides an overview, but more importantly, the opportunity to identify promising opportunities and developments. This way, we can monitor and accelerate the flow within the knowledge cycle. This requires leadership and coordination.

OPPORTUNITY 1

Faster implementation of solutions for patients

- Involving patients and their families as collaborators in all phases, from scientific research to care practice;
- Accelerating the knowledge cycle by fostering entrepreneurship.



OPPORTUNITY 2

Combining knowledge on disorders

A holistic view of the unique patient

Every patient, every brain and every situation is unique. This makes brain and mental disorders complex diseases. Different genes, sex and gender differences and a range of social and/or physical conditions contribute to their development. There is uniqueness in diversity. That is why the Netherlands Brain Initiative is opting for a radical transformation. We are no longer using specific disorders as our starting point but are focusing on the patient's unique and inevitably complex situation instead. This requires a holistic view, looking at parallels between causes, underlying mechanisms, treatment of conditions and strengthening people's ability to recover. Transdiagnostic and transcending traditional boundaries where possible and disease-specific where necessary. We do not lose sight of the unique expertise of the different domains. They contribute to the complex and challenging puzzle that the Netherlands Brain Initiative aims to solve.

INTESTINAL PROBLEMS

Having a condition like Alzheimer's, Parkinson's, susceptibility to psychosis or bipolar disorder is challenging enough. Patients often suffer from gastrointestinal issues as well. This may sound like an additional inconvenience, but there appears to be much more going on. By growing mini-intestines from patients' cells, we can see which foods can make people with Alzheimer's, Parkinson's, susceptibility to psychosis or bipolar disorder feel better and be able to do more. And we can do this without placing a long-term burden on the patients.



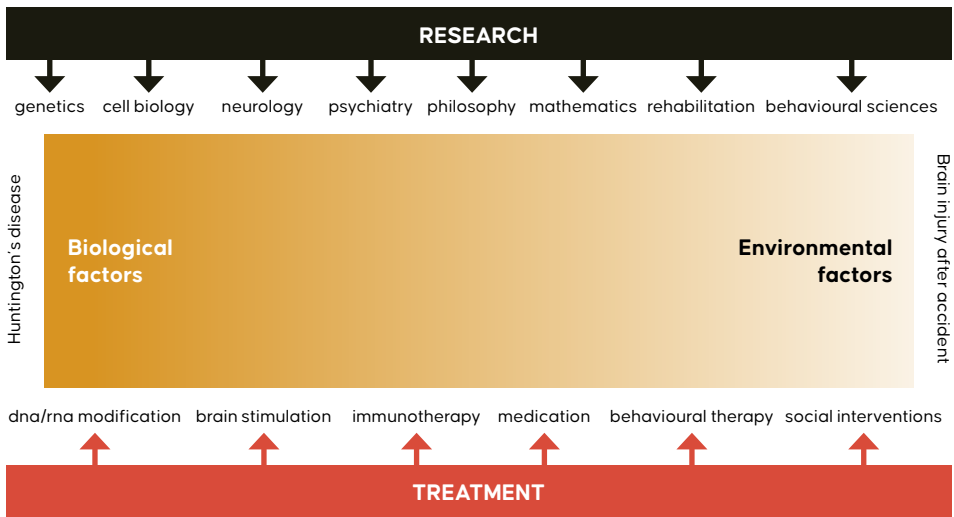


Figure 3: A combination of biological and environmental factors is often the cause of mental disorders of the brain. The extremes are Huntington’s disease (caused by a single abnormal gene), on the one hand, and brain injuries caused by accidents (caused by environmental factors), on the other. In fact, most brain and mental disorders are caused by a combination of biological, social and environmental factors. This is why the Netherlands Brain Initiative advocates a holistic approach to research and treatment (the research disciplines and treatments mentioned in the figure are, of course, examples and not exhaustive).

‘Gender and sex are routinely included and explicitly studied in mental health research. The scientific field is aware of the relevance of gender and sex to mental health and is more skilled in applying gender-sensitive science.’

Mission Alliance Gender & GGZ



*'Brain research focuses too much
on individual diseases'*

Patient survey the Netherlands Brain Initiative

Focus on the interplay of underlying mechanisms and circumstances

Brain and mental disorders are not a disparate collection of diseases. They affect the same organ, sometimes overlap, and sometimes occur together in the same patient. Despite the differences in the disorders, research on the underlying biological mechanisms often reveals the usual suspects. These include increased immune system activity in the brain, problems with blood supply, protein clumping, active stress systems and changes in the release of neurotransmitters or in the receptors for these neurotransmitters. In addition, a variety of social, physical and personal conditions play a role. It is also important to consider the influence of sex and gender differences on brain and mental disorders. All these mechanisms and factors are not isolated from each other. One influences the other. Just as the brain cannot be seen in isolation from all other organs. Research into the interplay of these factors will open new doors to prevention, treatment, better self-management and/or recovery from many brain and mental disorders.

Identifying and addressing inherited vulnerabilities

Neurological disorders often have a clear genetic risk factor. Psychiatric disorders, on the other hand, often involve a spectrum of small genetic differences that combine to determine hereditary predisposition. A person may be more or less prone to depression, anxiety and addiction, for example. Disorders often manifest differently between the sexes. The more we know about a gene palette in relation to such a cluster of disorders, the better we can map risk factors. This in turn allows us to develop new preventive strategies, for example.

Focusing on similar complaints

Many brain and mental disorders have similar symptoms in terms of energy loss, movement, behaviour, emotions, perception and thinking. For example, Parkinson's disease can start with depression or anxiety. On the other hand, people with depression often display slow movements and slurred speech. Common symptoms such as fatigue, irritability, loss of interest and sensitivity to stress overlap a lot. Or they overlap within gender. More attention needs to be paid to innovative, integrative research methods for treating these conditions. There is a need for recovery and learning to cope with the consequences of brain and/or mental illness.



RESEARCH ON SOCIAL WITHDRAWAL

Social withdrawal is often one of the first symptoms of different mental or neurological disorders, such as depression, susceptibility to psychosis and Alzheimer's disease. What happens in the brains of people who withdraw from their social environment, work, family or friends? That is what researchers from around the world, including the Netherlands, are investigating in PRISM (Psychiatric Ratings using Intermediate Stratified Markers) Ultimately, this information could speed up the development of new drugs for people with depression, susceptibility to psychosis or Alzheimer's disease.

More tailored treatment and lifestyle interventions

Many patients suffer from multiple conditions (comorbidity). These people are often not included in research, for example on drugs or non-drug treatments, because these other conditions may influence the research results. By not including these patients in research, research results are limited in their application. This means that we need to move much more towards personalised medicine and treatment. This will make it possible to look directly at what works for whom, regardless of whether it concerns one or multiple disorders. At the same time, by combining data, we can generate personalised prevention recommendations, such as lifestyle interventions that are important in preventing brain and/or mental disorders.

'As we are a small patient group compared to other brain diseases, a broad approach to the brain offers the greatest chance of increasing knowledge and opportunities for improvement for our patients.'

Patient survey the National Brain Initiative

Establishing long-term consortia

A long-term programme should also lead to more in-depth, translational collaborations, broad interdisciplinary consortia with long-term planning (10 years), using state-of-the-art techniques to study brain and mental disorders. In this process, the value of in-depth basic research is not forgotten. By involving people from across the healthcare chain, pooling their expertise and experience, we can create a breeding ground for innovative solutions and achieve implementation in practice. It is also important to invest in creative brainstorming with funders to work more across disorders and to do justice to the input of patients and their family members.

OPPORTUNITY 2

Combining knowledge on disorders

- Investing in research into cross-disorder similarities in symptoms, causes, underlying mechanisms and solutions;
- Developing new techniques for precision medicine and personalised lifestyle interventions.



OPPORTUNITY 3

Better sharing of knowledge and data

Specialists pool their knowledge and skills

By looking at people more holistically and studying processes in context, we can offer new solutions for people and science. Transdiagnostic and transcending traditional boundaries where possible, and (disease-) specific where necessary. Interdisciplinary work means pooling different layers of knowledge from, for example, molecular biology, neurology, neuropathology, ethics, behavioural science, sociology, psychology, psychiatry, rehabilitation science and nursing science.

Linking and analysing data

By standardising, harmonising, unlocking, combining and supplementing data at all levels with the experiences of patients and their families, new relationships can be discovered and new insights gained. Generic outcome measures are needed at all levels. In addition to all kinds of biomedical, genetic and neurological data, information about the patient's environment, gender, behaviour and perceptions can be a rich source for research into brain and mental disorders. In this way, we can learn to understand the huge puzzle of the brain and the influence of all kinds of factors on feelings and behaviour, for example. Not just piece by piece, but holistically and at different system levels.

Patients share data

Patients can also share and enrich all kinds of data with their own experiences. Using research methods such as EMA (ecological momentary assessment) and ESM (experience sampling method), patients can record all kinds of aspects of their lives with their condition. Databases of patient and family stories can be an important source of inspiration, both for other patients and families and for researchers. Online resources such as PsychoseNet.nl are needed to create a community and to disseminate experience knowledge widely.



CRISPR-CAS METHOD

Huntington's disease is caused by a mistake in the DNA that codes for the huntingtin protein. The abnormal huntingtin protein clumps together in brain cells. The brain cells deteriorate and eventually die. New genetic techniques make it possible to make changes to the DNA. The so-called CRISPR-Cas method can be used to cut pieces of DNA. This technique has already proved successful in other disorders. Researchers are currently investigating whether it can be used in Huntington's disease. As we learn more about the genetic basis of disorders, we can expect more breakthroughs for other brain-related disorders in the future.

Sharing and applying techniques

Disciplines can share knowledge on how to use the latest techniques for research and treatment. Growing brain cells, for example, makes it possible to study all kinds of processes, with more patient-specific results than in animal research, for example. The same is true of computer models based on human data. It is therefore necessary to share and harmonise technologies and infrastructures.

Organising networking and interdisciplinary communication

By organising a knowledge and innovation programme, we are laying an initial foundation for sharing knowledge and techniques between different disciplines. But more is needed. We want to create networks of researchers, patients, their families and healthcare providers. Joint conferences, journals, exchange of workplaces, development of web applications. In short, we want to create places and moments where all these experts and patients and their families (patient experts) can meet digitally or in person.

'Psychological suffering involves a complex set of experiences and conditions – from the existential to the “pain” of the past to the highly familial – that require a holistic approach. Dealing with it is a long and arduous learning process, and we can learn a lot from those who have already acquired this knowledge. It is great that the Netherlands Brain Initiative wants to use and leverage experiential knowledge as a resource in its own right.'

Prof J van Os, psychiatris

OPPORTUNITY 3

Better sharing of knowledge and data

- Encouraging collaboration and sharing of knowledge, techniques and data at all levels and between all disciplines;
- Organising networking and interdisciplinary communication.



Supporters of the Netherlands Brain Initiative

[Click here](#) for an overview of the people supporting the Netherlands Brain Initiative.

'The Netherlands Brain Initiative of the Brain Foundation Netherlands, MIND, ZonMw, NWO and Health~Holland identifies, integrates, stimulates, initiates and prioritises important trends in the field of neuroscience and related disciplines. Amsterdam Neuroscience of Amsterdam UMC, VU and UvA fully support this initiative in word and deed. There are many top young researchers in our institute who value a broad and patient-centred vision. By joining the Netherlands Brain Initiative, they could make an important contribution to a nationally supported vision in the field of translational neuroscience and clinical research into brain diseases.'

Prof A.B. Brussaard, neuroscientist, Amsterdam Neuroscience

'From 'policy headaches' to practical essentials: Top Sector Life Sciences & Health and its colleague Top Sectors are happy to contribute to the establishment and success of such a partnership. The sooner, the better!'

Prof. dr. Nico L.U. van Meeteren, executive director Top Sector LSH

Ambassadors of the Netherlands Brain Initiative

[Click here](#) for an overview of the ambassadors Netherlands Brain Initiative.

Colophon

The Netherlands Brain Initiative is an initiative of Brain Foundation Netherlands, MIND, ZonMw, NWO and Health~Holland.

The Netherlands Brain Initiative aims to bring together and share knowledge and data on brain and mental disorders so that solutions for patients are implemented faster into practice.

This manifesto was created with input and advice from various patient organisations, experts with practical knowledge, doctors, scientists and researchers.

www.netherlandsbraininitiative.org



Help us **tackle brain and mental disorders.**

Join us in **making this a top priority!**