DONDERS INSTITUTE

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Anxiety and resilience during the pandemic

When COVID-19 led to the Netherlands going into lockdown in March 2020, two Donders research teams looked at their current research projects and decided that they could make unique discoveries just with some minor adjustments. There has been a great deal of speculation on the negative impacts of the pandemic on mental health. Neuroscientists Anne-Kathrin Brehl and Sophie Bögemann, who investigated this, report on the outcomes of their research projects. What did they discover?

At the start of the pandemic, Anne-Kathrin Brehl had just completed a study involving 250 people who scored high on anxiety scales but did not fulfil the diagnostic criteria of an anxiety disorder. She quickly realised that these pre-pandemic data could be very useful for comparison in a follow-up study. She contacted the participants and sent them regular online surveys to ask about their anxiety, stress, and depression levels over the past year.

"I wanted to see if people's anxiety level before the pandemic could predict how they were to deal with this situation. The prediction was that the participants would experience even more symptoms of anxiety during the pandemic."

CHANGING THE PLAN

For Sophie Bögemann, April 2020 was planned to be the start of a large consortium project on mental resilience called DynaMORE. The plan was to approach this subject multimodally by looking at brain function, genetics, the gut microbiome, and daily life measures at the physiological and psychological level. But as both researchers and participants were not permitted to go to a lab, this approach was no longer viable. "We realised that this pandemic was also a huge opportunity for us, because suddenly people around the world are facing the same extremely severe stressors. We wanted to find out how people deal with that stress and what makes some people more resilient than others."

The aim of the DynaMORE research project is twofold. "First, we gave a multi-lingual survey to 15,000 participants so that we could assess their mental health and stress exposure. We hypothesised several psycho-social factors which we thought would be protective for mental health. Examples of these resilience factors are positive appraisal style, general self-efficacy, perceived social support, and behavioural coping style."

"Later, we did a second study. We followed a smaller group of 500 people for six weeks, and we asked them every week how they felt, what stressors they encountered during that week and how they dealt with them."

COPING STRATEGIES

Although Brehl and Bögemann were investigating different aspects of mental health, their studies complement each other, as do the initial outcomes.

Brehl – who had made a baseline measurement before the pandemic – found that the participants' anxiety appeared to increase only slightly. "We discovered that anxiety levels before the pandemic did not determine how anxious a person was during it, but the way people usually regulate stress and other negative emotions did. In psychology, it's possible to distinguish between adaptive and maladaptive emotion regulation strategies. Those with maladaptive strategies were more anxious. So, people who, for example, give up easily or blame themselves tended to be more anxious."

"One exciting finding, though, was that people who usually deal with their anxiety symptoms by avoiding contact with others, felt less anxious during the first lockdown. This maladaptive strategy of social withdrawal – which is usually considered a 'bad' coping mechanism – was now of help rather than a hindrance."

Bögemann investigates resilience, which the consortium defines as the maintenance or recovery of mental health despite exposure to stressors. "We look at mental health effectively, but we correct for the stressors that someone encounters. As we predicted, the psycho-social protective factors were positively associated with resilience."

"When we followed people every week, our preliminary results showed that for most factors there is a positive association across all participants across all time points. Interestingly, we found that specifically positive appraisal style and general self-efficacy could also fluctuate with resilience per week for a single participant. So, one week someone believed in their capability to handle the situation or see the positive side, which made them more resilient. But the next week, they weren't using these protective factors and felt more stress."

And so, Bögemann's research shows which factors might strengthen people's mental health, whereas Brehl's work shows which factors could worsen mental health, specifically stress and anxiety.

ON-GOING PROCESS

Both researchers stress that their results are related to the first wave of the pandemic, which took place in Europe from March to June 2020. Both research teams continued collecting data and are still doing so. They will soon, therefore, have more results and be able to determine if their results hold up in general or differ depending on the circumstances.

Brehl will be glad when she can get back to her project objectives as originally planned. "In psychiatry, patients with similar anxiety symptoms are often given similar treatments. However, treatment success rates of state-of-the art treatments vary considerably between individuals, even though they have the same symptoms. I want to investigate the various biological mechanisms that might explain this discrepancy. I like to work on the crossroads between psychology and biology."

Bögemann and her colleagues are now back in their labs again and are doing the multi-modal research as planned. "I find resilience super interesting, and we have so many more unanswered questions. I hope my research can identify mechanisms that will help people stay mentally healthy in stressful times and prevent people from suffering mental disorders. If we can discover protective factors, perhaps we can train people to stay resilient when life hits them hard."

Brehl adds: "It's not about *not* feeling stressed or anxious. You can still function fine with these feelings. Good mental health is about how you deal with negative emotions and situations."

Vanessa Deij

The never-ending search for surprises

FLORIS DE LANGE WANTS TO KNOW HOW OUR BRAIN DEALS WITH THE UNEXPECTED

Imagine entering your living room only to find that your good old white walls have suddenly turned dark red. How does your brain process this unexpected observation? Cognitive neuroscientist Floris de Lange studies how our brain makes predictions. He now wants to know what happens when those predictions don't come true. This academic year he received an Ammodo Science Award and an ERC Consolidator Grant to extend his research in this direction.

We do many things as if we're on autopilot. According to Floris de Lange, this can be explained by considering our brain not as an information processor, but as a prediction machine. According to this view, the brain is constantly trying to predict incoming information. What we expect to see, hear, feel, and smell, but also what the consequences will be. De Lange: "This is useful for survival. If you can successfully predict what another individual intends to do, that will give you a huge advantage."

INVALUABLE SKILL

This is a never-ending process, which takes place in all brain systems, from the sensorimotor system to the language faculty. For example, you predict where to put your feet when you walk up the stairs, you fill in missing characters while reading and you walk round a puddle to avoid getting wet shoes.

The ability to predict the environment also has other advantages. "Predictable events require little processing, and therefore little energy. Processing unexpected information is much less energy efficient. Since our brains consume about a quarter of our total energy supply, energy efficiency is essential."

So predictions that come true are, in a sense, muffled. That doesn't apply to surprises - the moments when your brain's expectations were proved wrong. "We see a lot of activity in the visual cortex when people see something they didn't expect. The same is true for unexpected sounds, when we hear a tone of unexpected pitch in music, for example. But surprise is not limited to sensory systems. What processes are triggered by surprise in the brain? And how do we process surprising information?"

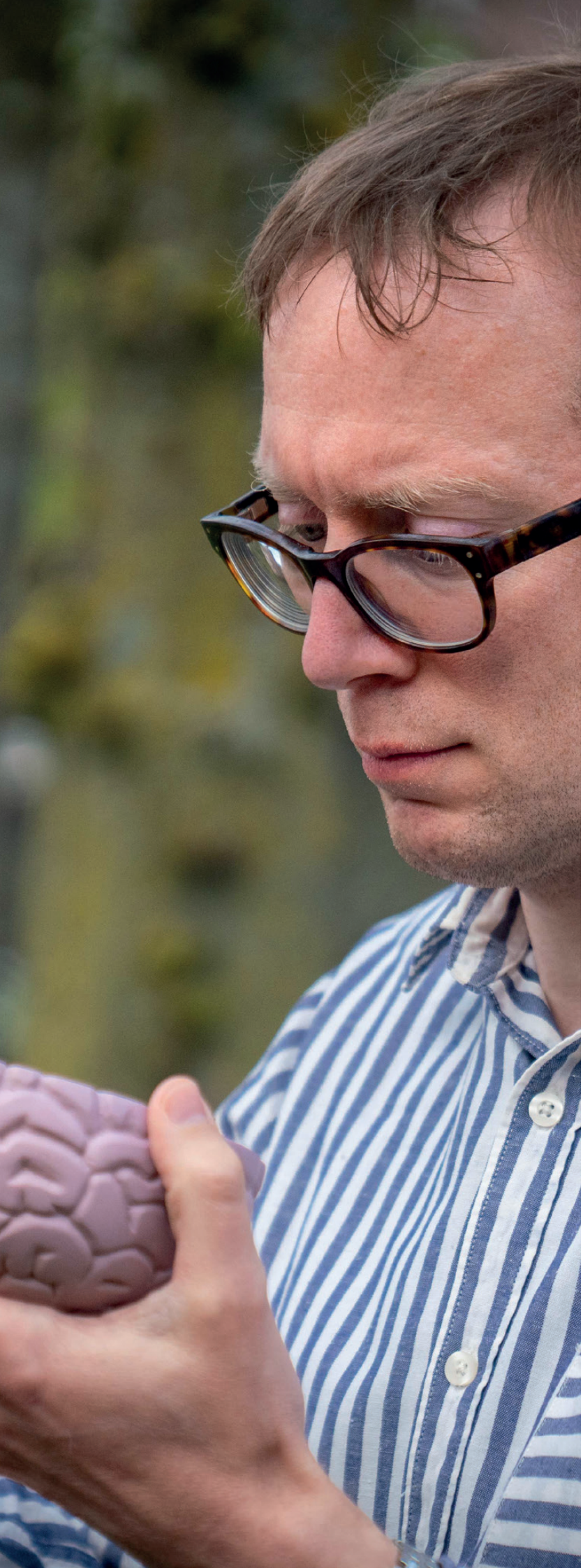
FROM SURPRISE TO EXPECTATION

In his new research, which is funded by an ERC Consolidator Grant, De Lange is looking for the consequences of surprises. One of the premises is that these are important moments. After all, a surprise means that your predictive model is incorrect.

Based on unexpected observations, your brain will likely update its predictive model. "If those white walls in your house are suddenly painted red, you'll be surprised at first. And maybe a little angry with your partner. But the next day you'll be much less surprised when you open the door and get confronted with that colour again. After a few times the model is completely up to date and you don't notice it anymore."

This also happens in everyday situations: a car that appears out of nowhere or a dog walking by. After being surprised in this way on several occasions, you will learn to anticipate similar situations. The principles are the same. De Lange wants to find out how sensory surprises trigger updates to our world model. Are we more attentive if we have just been surprised? Is our curiosity triggered?

To investigate this, research participants are shown a series of images in an MRI scanner, as if they are browsing through a photo book. These are shown in a fixed order, without them realising it. " When you give volunteers a different task, looking for certain images for instance, they will often not consciously realise that the pictures always appear in the same order. But the order is implicitly learnt. We clearly see more brain activity when we suddenly change the order.



"We do not know if surprise is limited to specific visual or auditory brain regions"

HUNGER FOR KNOWLEDGE

Another assumption is that people are driven by the urge to acquire knowledge. Not necessarily because this might make them happy. But perhaps mainly because it can be an unpleasant feeling when you don't know or can't do something. "Compare it to hunger: eating can be satisfying but being hungry definitely is an unpleasant feeling you will try to eradicate."

This natural hunger for knowledge creates a state of curiosity. De Lange wants to find out whether curiosity is triggered by situations in which a prediction turns out not to be correct. "We already know that surprise leads to more brain activity. We do not know if this is limited to specific visual or auditory brain regions, or whether it also leads to more attention. When you're browsing through that photo book and you come across something you don't expect, does this mean that you will automatically pay more attention to that photo or to the photos after it? Perhaps you are expecting more surprises? That, too, may be a form of curiosity: anticipating surprises."

Thanks to an Ammodo Science Award, De Lange is in a position to set up an additional research project. Unlike the ERC grant, he can use the prize money of €300,000 for a research project that can still be defined. "I am considering using the Ammodo Award to find out why we search for certain information. What makes us eager to look for specific knowledge? This also relates to the hunger for knowledge and it ties in with curiosity."
Roeland Segeren

Newsflash

- **Real-time dialogue with a dreaming person is possible**
  Dreams take us to what feels like a different reality and they take place while we're fast asleep. So, you might not expect that a person in the middle of a vivid dream would be able to perceive questions and provide answers to them. But research now shows that, in fact, they can. This study by Martin Dresler, in collaboration with an international group of researchers, was published in Current Biology.

- **US$1.4 million to bring research on retinal disease into the clinic**
  Rob Collin and Carel Hoyng have received a prestigious award from the Translational Research Acceleration Program (TRAP) of the Foundation Fighting Blindness USA. With this three-year award, which is worth US$1.4 million, the researchers aim to bring a new therapy for patients with Stargardt disease up to the phase of clinical testing. The procedure, called antisense oligonucleotide-based splicing modulation, repairs defective transcripts in the human retina that underlie blindness or significant loss of vision. Collin is one of the researchers who pioneered this method for use inside the eye.

- **Real-life brain cells attached to a computer engage in continuous rivalry**
  The brain continuously receives noisy – and often ambiguous – information. How does the brain process this into a clear perception of the world? For this purpose, it has been assumed that the brain chooses among competing signals. Naoki Kogo investigated this so-called neural competition by attaching two brain cells to a computer. He found that they 'fired' in turn. This resembles what happens when people experience an optical illusion, called bistable perception. The findings were published this month in the Journal of Neuroscience.

- **Three Donders researchers become professors**
  Lisenka Vissers, Corina Greven and Vivian Weerdesteyn have been appointed as professors by the Radboud university medical center (Radboudumc). They are part of a group of 13 new female Radboudumc professors, which brings the percentage of female professors there to thirty percent. Corina Greven has been appointed as Professor of Environmental Sensitivity in Health, Vivian Weerdesteyn as Professor of Motor Control and Rehabilitation and Lisenka Vissers as Professor of Translational Genomics.

- **You don't have to be a genius to develop a strong memory**
  Memorising items by visually putting them in a familiar environment is an established technique that successfully helps people to memorise names, numbers, a shopping list, or even a big set of data during memory championships. Training the brain with this so-called 'memory palace' even improves longer term memory, as Boris Konrad and his colleagues recently discovered. They published their findings in Science Advances.

- **Scientists link genes to brain asymmetry**
  The left and right sides of our brain have different functions. But what is the genetic basis of this left-right asymmetry? In a large-scale genetic study, scientists from the Max Planck Institute and Donders Institute in Nijmegen and the University of Bordeaux found fifty-seven genes connected to human brain asymmetry. These genes are especially active during prenatal brain development. Moreover, there was also an overlap with genetic variants associated with psychiatric disorders and educational attainment.

PhD defences

November 2020 - December 2020

- **Dirks, M.F.M.,** *Neural mechanisms of Parkinson's tremor.*
- **Mendes Diniz, D.,** *Unravelling the role of brain-derived Neurotrophic Factor in depression. BDNF overexpression in Serotonin Transporter Knockout Rats.*
- **Lith, B.J.H. van,** *Balance and gait problems in people with hereditary spastic paraplegia: patient experience, underlying mechanisms, and clinical management.*
- **Wu, Z.,** *The functional and structural brain alterations in ADHD and their genetic correlates.*
- **Berenpas, F.,** *ACTIVE neuroprosthesis for people with drop foot after stroke: GAIT, muscle and foot nerve.*
- **Kirkels, L.,** *Visual Motion Integration in Mice and Men.*
- **Dalmay, T.,** *The role of temporal neocortex in threat memory.*
- **Spiess, L.,** *Who are you, and how many? The role of Individual Knowledge and Group Knowledge in Social Predictions.*
- **Tyborowska, A.B.** *Shifting Control. Neurodevelopment of emotional circuits during adolescence.*
- **Lôpo Polla, D.,** *Molecular approaches to decode intellectual disability syndromes.*
- **Zeetsen - Bruijnen, C.J.W.H.,** *Substance-Induced Neurocognitive Disorders detection, prevalence and course during treatment in addiction health care.*
- **Eijk, J.J.J.,** *Antecedent infections in neuralgic amyotrophy, a prominent role for hepatitis E virus.*
- **Janssen. N.,** *Staying connected as we speak: Behavioral and tractography evidence from health and neurodegenerative disease.*
- **Vijayakumar, S.,** *Principles of parietal-frontal cortical organization.*
- **Buric, I.,** *Individual differences and psychobiological responses to mind-body interventions.*
- **Linda, K.,** *Modeling neurodevelopmental disorders using human pluripotent stem cells: from epigenetics towards new cellular mechanisms.*
- **Lassche, S.,** *Contractile function in facioscapulohumeral muscular dystrophy.*
- **Haaften, L. van,** *Profiling typical and disordered speech production in children using the Computer Articulation Instrument (CAI).*
- **Heesterbeek, T.J.,** *Risk factors for progression of age-related macular degeneration.*
- **Van Es, M.,** *On the role of oscillatory synchrony in neural processing and behavior.*
- **Van Dongen, L.,** *Cognitive and psychopathological phenotyping of rare Mendelian disorders: Towards a neuropsychological algorithm.*
- **Roelofsen, E.G.J.,** *Neuromotor Flexibility Following Musculoskeletal Leg Injury.*
- **Tengeler, A.C.,** *Mind the microbes. The impact of the gut microbiota on brain structure and function in mice. (Cum laude).*

An eye-catcher with teething troubles

One of the Donders Institute research centres has recently moved to the new Maria Montessori building. Researchers are in general happy with the new facility, although there have been some teething problems.

One of the remaining old, grey, communist-like buildings at Thomas van Aquinostraat is now a silent reminder of the past. Although this one still stands, inside it's empty. One of the rooms in the building served as the technical heart of the Faculty of Social Sciences. Technical Support Group members, Norbert Hermesdorf and Gerard van Oijen, spent much of their time there.

However, the times they are a-changing. The current workspace of the duo, in the new Maria Montessori building, is modern, brightly lit and surrounded by glass walls from top to bottom. 'It's a beautiful new building, so we're happy that we moved. However, I must say that it's still clearly early days', Van Oijen said.

TEETHING TROUBLES

A couple of weeks ago, a technical engineer tested the "sled" (a high-tech chair used for research). 'But, when I recently rechecked it, there were problems with the voltage, perhaps because someone had made changes to the electricity network in the building,' Hermesdorf observed. Recently, a planned test required the electricity to be shut down for a night. 'By coincidence and with a good bit of luck, we found out about the shutdown. If not, it would have been a disaster for some of the ongoing research, as certain machines need a constant energy supply,' Hermesdorf said.

Apart from these teething problems, they greatly appreciate the new building. The hardware has been renewed and the cabins have sufficient headroom for the cameras to film the research better. In most spaces, the research can be carried out in a separate room from the experiment itself.

MODERN OUTLOOK

"The Iris", the canteen, is an eye-catcher. Immediately after entering the building and climbing the stairs, you come across this state-of-the-art hall, decorated like a forest with many glass walls. The space is decked out with at least forty large plants, including two colossal ivy vines, each about four metres high. 'During my study, I had courses in the old, dark building', says researcher Rosemarije Weterings. 'It was always a quest to find where the course room was. Compared to that, the new building is brightly lit, greener and much more transparent,' she added.

Daan Appels

THE MACHINE

Scientist in a duel with mother nature

Martijn Agterberg investigates the behaviour of bumblebees in a mobile laboratory next to his house. He expects to use the information to improve the design of human hearing implants. However, the bees continue to outsmart him, despite his best efforts.

Agterberg has learned to embrace failure graciously. Sometimes, a failed scientific experiment will lead to something even more beautiful. For months, working in the mobile laboratory, he tried to manipulate bumblebees' behaviour and landing accuracy. In a Pavlov-like experiment, he aimed to teach the insects to fly towards a reward – glucose in this instance – inside the mobile lab.

Unfortunately, the force of nature overpowered his artificial reward. The bumblebees wanted only one thing: to get out and search for flowers. The fact that he was not able to manipulate them confirmed the creatures' intelligence. 'Although it was disappointing in the beginning, this is a fact that I learned to love later on,' Agterberg said.

ON A SOUND MISSION

He's also studying the movement of the bumblebees' antennas. Halfway along their antennas, they have a collection of sensory cells called the "Johnston's organ", which acts as the bees' ears. The bees can move their 'ears' towards and away from each other. The hypothesis is that bees can localise sounds because they can move their ears. Should Agterberg's theories prove accurate, then the goal will be to build a biological mechanism (a directional sensor) into hearing implants. Despite all the hurdles he's faced, this scientist has not given up and continues his study using several research setups.

The mobile lab consists of a plateau for the commercial hive and sensitive cameras that can capture high-frequency wing movements. It also has high-quality music boxes that can produce low frequencies driven by custom-made software.

At its peak, about 500 bumblebees lived in the lab. The hive is as big as a fish stall, so Agterberg had to acquire a special license to drive the lab to his house. 'That is not the only sacrifice I made. I also got stung on my foot. It got very, very swollen,' he said. Agterberg added with a big smile, 'But I don't blame the bees, because I made the mistake of going into the lab wearing wooden clogs.'

Daan Appels

DONDERS INSTITUTE Newsletter

The Donders Newsletter is published twice a year by the Donders Institute for Brain, Cognition and Behaviour, which brings together research groups at Radboud University and the Radboudumc as well as the Max Planck Institute for Psycholinguistics. Its purpose is to keep you informed of developments within the Donders Institute and the wider field of neuroscience.

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