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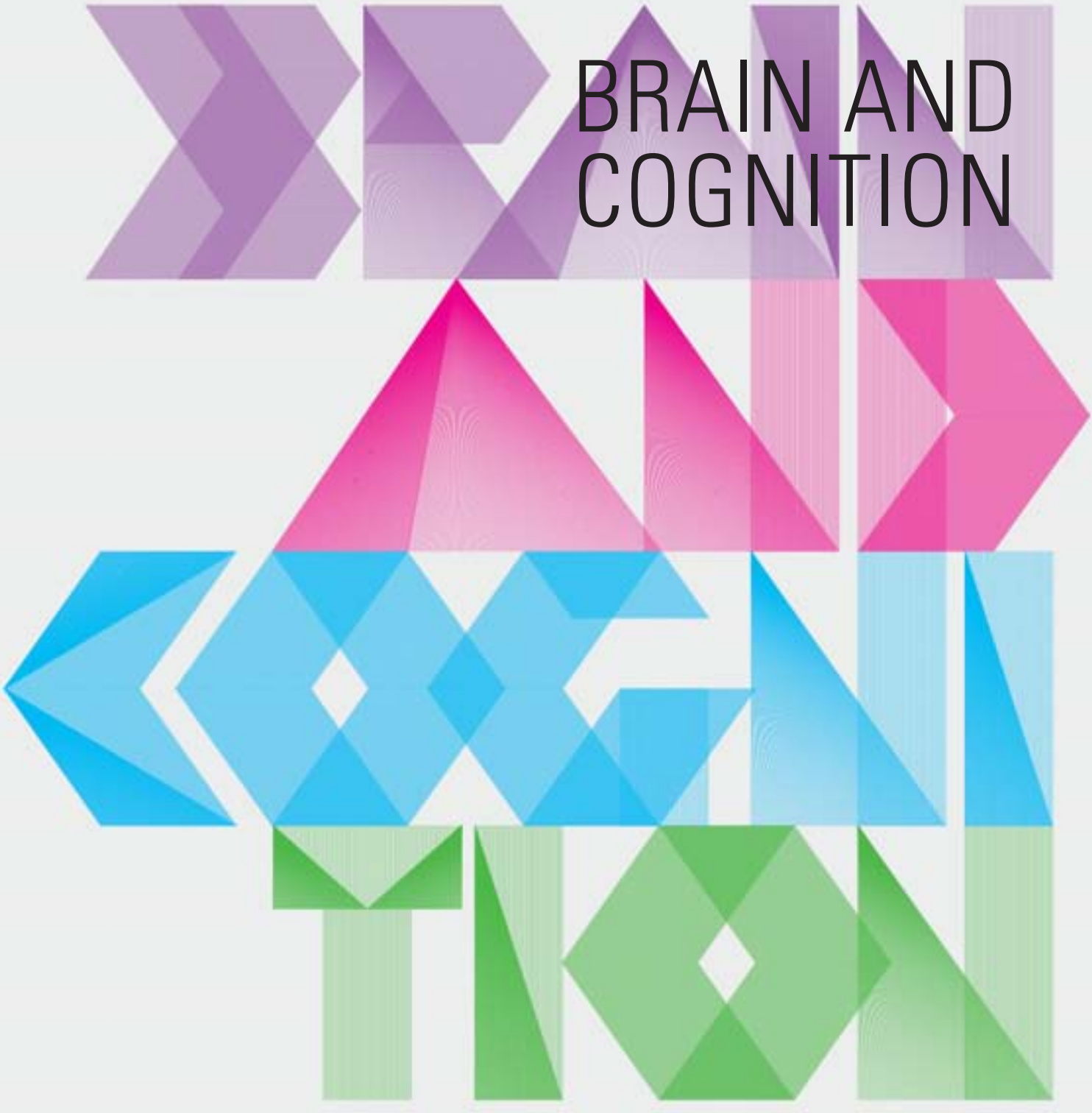
Number 5 – Summer 2010

BRAIN AND COGNITION



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Founding Mother
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EDITORIAL

Deep sea diving

by Vittorio Busato

'When I know something, I can predict something; when I can't predict anything, I don't know anything.' Thus goes the adage by the late Adriaan de Groot, professor of methodology in psychology at this university until the mid 1970s and still one of the Netherlands' most renowned psychologists.

The theme of this issue of MindOpen is the university research priority program Brain & Cognition, a collaboration between the Faculties of Social and Behavioural Sciences (FMG), Science (FNWI), Humanities (FGW), Economics and Business (FEB) and the Academic Medical Center (AMC) of the University of Amsterdam. This priority program will officially kick off on September 14, 2010, with a symposium in the P building of the Roeterseilandcomplex, where new workspace has been created for the researchers involved. Four ambitious research programs are central to this UvA-wide inititative. In short, these projects focus on 1) what is consciousness; 2) how do young children learn to categorize sounds, objects and social emotions; 3) which neurocognitive mechanisms are at the basis of (impulsive) decisions and 4) how can fear be erased from memory.

Those are ambitious questions. And although the researchers have certainly formulated predictions they can test empirically, among others through the latest brain scan techniques, this university research priority program can partly be characterized as deep sea diving; they will most certainly be surprised at what they'll encounter along the way, by that which they cannot predict. As Paul Boersma says, in this *MindOpen*: 'Although our project involves basic science research, part of it could most certainly be characterized as exploratory. That's why, frankly speaking, I don't have very concrete expectations, other than that as researchers from different disciplines we will certainly learn a lot from each other.'

I think it's the combination of "hard" and explorative research that makes this priority program, this journey of discovery, so special. This issue of MindOpen chronicles the beginning of that journey. And if there's anything I would dare to predict, it's that in the future we'll see travel accounts about the fascinating discoveries this interdisciplinary collaboration will doubtlessly yield.

Vittorio Busato
editor

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PREFACE

University Research Priority Program Brain & Cognition

by Gerard Kerkhof

The past thirty years have shown an impressive growth in knowledge in the area of cognitive sciences. We've seen this growth both at the level of the neurons and neural systems involved, as well as at the level of the regulation of behavior, the theoretical modeling of behavior and insight into cognitive disorders. Research in the area of cognition is very well represented within several faculties of the University of Amsterdam (FMG, FNWI, FGW, AMC, FEB) in research teams that include psychologists, neurobiologists, neurologists, psychiatrists, behavioral economists, logicians and linguists. These groups get high visitation scores, averaging between 4 (very good) and 5 (excellent). They also have a very strong national and international profile, as evidenced by the large number of grants from organizations such as NWO and the large number of international publications.

Cognitive researchers from the UvA regularly run into each other during overseas conferences and find to their surprise that they share the same overarching research theme, although they approach it from different angles. This shows that there are still plenty of opportunities for collaboration, especially collaboration that is focused on increasing the understanding of interactions between different levels of cognitive activity. Research into this area requires an interdisciplinary approach, for which the UvA UvA offers extraordinary opportunities.

In 2008 the Executive Board of the University of Amsterdam founded a university research priority program to strengthen the university's position as a member of the League of European Research Universities (LERU). This program has been enthusiastically used by the Cognitive Science Center Amsterdam (CSCA)—which already has faculties collaborating on an interdisciplinary two-year Research Master's program in cognitive science—to shape the much-needed interdisciplinary collaboration in the area of research, too. The Executive Board has decided to designate Brain & Cognition as the university's first research priority program and to fund it from the central UvA strategic budget, supplemented with funds from the five faculties involved. This decision was influenced, among others, by the fact that, on the one hand, several UvA faculties house many excellent cognitive scientists and, on the other hand, by the consideration that a strengthening of the mutual interdisciplinary collaboration would not only mean a significant step ahead, but would also increase the international visibility of the cognitive research at the UvA.

The goal of the priority program Brain & Cognition is to establish an internationally visible and leading institute at the UvA that maintains a worldwide network of prominent cognitive researchers and is a breeding ground for groundbreaking ideas and developments in the area of cognition. It will achieve this by stimulating international collaborative efforts around interdisciplinarily oriented cognitive themes, thus increasing the international visibility of the cognitive research at the UvA, both in and outside of academia; attracting and retaining leading scientists and young talent and supporting them in conducting ambitious research and publishing in top journals; and finally, obtaining large-scale (European) grants that can be used to maintain a top-ranked international cognitive network.

This special edition of MindOpen lays out several ambitious research plans that will be implemented within the research priority program Brain & Cognition. In interviews and background stories with the researchers involved they explain which questions shape their research—questions such as what exactly consciousness is; how young children learn to categorize sounds, objects and social emotions; which neurocognitive mechanisms are at the foundation of impulsive decisions; and finally the question how fearful memories can be erased.

These are just a few of the many cognitive themes being researched at the UvA. In years to come, these projects will be implemented, and other cognitive scientists within the UvA will also be involved where possible in the research priority area Brain & Cognition.

Gerard Kerkhof
Director Brain & Cognition

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IN SEARCH OF A NEW TREATMENT FOR PTSD

by Jorn Hövels

Long-term memory is less unerasable than scientists have always thought, according to recent research. Negative emotional memories can be influenced shortly after they have been reactivated. This creates new opportunities for the treatment of anxiety disorders and post-traumatic stress disorder (PTSD).

Among other things, these opportunities are being explored in the research program Keeping emotional memories at bay: from molecule to patient, one of four projects awarded in the university research priority program Brain and Cognition. The project is jointly led by Merel Kindt, professor of experimental clinical psychology; Marian Joëls, professor of neurobiology; and Miranda Olff, head of the AMC's psychotrauma research program. The goal is to better understand the emotional memory and find out how unwanted emotional memories can be weakened in patients with an anxiety disorder or PTSD. The ambitious research project needs to bridge different disciplines. Using animal research, Joëls' research group primarily studies the fundamental neurobiological principles of memory. Kindt's program group focuses on, among others, the emotional memory functions of healthy volunteers. Olff predominantly focuses her research on the potential applications for the treatment of patients.

'This joint project is a unique collaboration,' Kindt says. 'Take Joëls' research. She has the opportunity to inject the substances propranolol and cortisol—both of which influence the emotional memory—directly into the amygdala or hippocampus of rat brains. Such animal experiments, which are not within my reach, yield a variety of new insights for us. This advantage also goes the other way around. In our research with healthy volunteers and patients, Olff and I can differentiate between different types of memory. Moreover, it's important to eventually test findings from animal models in humans.'

"OVERWRITING" FEAR MEMORIES

Since the nineteenth century psychologists and psychiatrists have tried to change unwanted, fearful memories with therapies and drugs. Until recently, their efforts were in vain—memories appeared to be permanently fixed in long-term memory. The assumption was that fears of patients with anxiety disorders or PTSD had also been inerasably fixed in their memory.

Right now, the most common and effective treatment for patients with an anxiety disorder is cognitive behavioral therapy. For anxiety disorders, this consists of exposure—the repeated confrontation of patients with fear-inducing stimuli such as a spider, a dog or air travel. This gradual and repeated confrontation causes the fear response to eventually weaken or even extinguish. This is because this treatment enables patients to experience time and again that feared consequences fail to occur: the spider does not attack; the dog is strokable; the plane lands safely.

Exposure treatments are quite effective. However, if a patient has rather complicated or severe traumas, the anxiety symptoms—such as insomnia, flashback episodes, nightmares, problems focusing—can return in time. Kindt: 'During exposure treatment, patients create a new memory pathway that suppresses the old one. But the old fear memory stays intact and can eventually start to dominate again.'

The three scientists are therefore looking for ways to actually change fear memory; ways to "overwrite" the old memory instead of suppressing it. Olff: 'We're striving for an anxiety treatment with one hundred percent results. But I do want to emphasize that our project involves basic research. Our primary focus is to better understand the emotional brain. Who knows—we may eventually come to an ideal anxiety treatment and develop a treatment that works faster or is easier to provide than cognitive behavioral therapy. Anything we can do to relieve patients of their nasty post-traumatic stress complaints either sooner or more efficiently is worth the effort.'

MEMORY CHANGES DURING RECONSOLIDATION

The most important reason to apply for research funds for this ambitious project was earlier research by Kindt and her doctoral student Marieke Soeter, which they published in the journal Nature Neuroscience in 2009. This research showed that subjects' emotional fear response disappears permanently if they are given the beta blocker propranolol just prior to the reactivation of their fear memories. This is a drug that is normally prescribed for high blood pressure and heart disease. Various artists also use it (in low doses) for stage fright.

Kindt: 'Contrary to what has long been thought, neuroscientists are finding more and more clues that raking up old memories again plunges the memory pathway back into an "unstable condition." This memory pathway can subsequently be consolidated again. This process is also referred to as reconsolidation. The beauty of this is that during this short time—this supposed reconsolidation phase—we can intervene in the memory pathway. You can strengthen the old memory pathway, something new can be learned, and fear memories can be weakened.'

While disrupting the reconsolidation it is important that it is the emotional fear responses that change and not the memories themselves—those are stored in the declarative memory. People need to still be able to remember, for example, that some dogs are dangerous, or that it is risky to be sent to Afghanistan as a soldier. That's why it's quite possible that, in the future, patients will be faced with a difficult choice: do I want to get rid of my anxiety, or do I want to save all the details of my memory? Kindt: 'There are studies that show that propranolol also affects the declarative memory. That makes sense—when emotions dull down, people remember details less vividly.'

With her animal models, neuroscientist Joëls studies the fundamental neurological mechanisms that play a role in the stirring up and weakening of fear memories. Her research group focuses on, among others, the influence of stress hormones such as cortisol on memory storage. The effect of the stimulating neurotransmitter glutamate on the extinguishing of fear memories is also being studied more closely by her group.

Joëls: 'We want to know how different drugs can intervene in the fear memory. In animal models we can intervene very precisely in parts of the memory process and discover which steps are essential in that process. That gives us new ideas for treatment that we can subsequently test in humans.'

DO I WANT TO GET RID OF MY ANXIETY, OR DO I WANT TO SAVE ALL THE DETAILS OF MY MEMORY?

SLEEP AND MEMORY

In collaboration with the sleep lab of researcher Lucia Talamini of the psychonomics program group, Olff's research group will look into how sleep is disrupted in PTSD patients. During the night, many patients with PTSD are still fleeing things that once happened. They have nightmares, repeatedly wake up with a start, and experience flashback episodes. Olff: 'We don't yet exactly know what effect that has on memory, but we suspect that in addition to the trauma disrupting sleep, sleep patterns also influence the ability to cope with trauma.'

It has been known that after exposure therapy or after taking medication the brain activity of PTSD patients during sleep is different than before. Olff: 'If we can discover how we can improve the sleep of PTSD patients, that would already be quite something. Or, the other way around, that improved sleep allows them to better cope with the trauma. We'll have to research that, too.'

Kindt, Joëls and Olff are not the only researchers looking at anxiety. Agnes van Minnen, endowed professor of anxiety regulation at the Radboud University in Nijmegen, has previously done research on exposure therapy for PTSD patients in combination with d-cycloserine, a drug that is being thought to have a facilitating effect on extinction. After taking d-cycloserine as part of exposure therapy, patients are said to remember even better that they don't have to be afraid of fear-inducing stimuli.

Beside the fact that Kindt thinks treatment results with d-cycloserine are disappointing, she is especially worried about the (too) rapid application of new treatment methods. 'D-cycloserine is a dangerous drug. When you rake up an emotional fear memory, you run the risk of strengthening the old fear memory, instead of the newly learned.'

Such risks also apply to a drug like propranolol. Still, patients are already being treated with it abroad. 'I wouldn't feel comfortable doing that yet,' Kindt says. 'While we're using the drug to weaken the old memory, in the case of propranolol it could also happen that during the treatment the newly learned is accidentally being weakened. The drug would then have the opposite effect. You have to be very careful with such drugs and should not use them to treat people right away.'

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Merel Kindt


Marian Joels


Miranda Olff

LONG-TERM MEMORY IS LESS UNERASABLE THAN SCIENTISTS HAVE ALWAYS THOUGHT

Saving fear memories as a text file

by Jorn Hövels

Clinical psychologist Marieke Soeter has been working on her dissertation for three years now. With her dissertation supervisor Merel Kindt, professor in the clinical psychology program group, she published the article "Beyond extinction: erasing human fear responses and preventing the return of fear," in the top journal *Nature Neuroscience* in 2009. This research shows that a fear response in subjects disappears permanently upon reactivation of their fear memory if they've been given propranolol immediately prior. Soeter: 'Compare it to retrieving, revising and resaving a text file.' The research opens up new perspectives for the treatment of patients with post-traumatic stress disorder (PTSD). The results were part of the reason for the grant proposal for the sizeable research project 'Keeping emotional memories at bay: from molecule to patient.'

How did the research go?

'On the first day, we conditioned the subjects to learn a fear. They were shown images of spiders, one of which was followed by an electrical shock to their lower arm. On the second day—24 hours later—we reactivated the conditioned fear. The subjects were again shown the image that had been accompanied by an electrical shock a day earlier. Prior to the experiment on the second day, half of the subjects were given propranolol. We gave placebo to the other half. The conditioned fear was measured on the third day by means of the so-called startle fear response, a fright reflex that is initiated by the amygdala—the fear center of the brain—and is a good indicator of fear. It turns out that subjects who had been given propranolol on the second day were no longer afraid on day three of the spider image that had been accompanied by the electrical shock. Their fear response had disappeared. We saw the same result a month later. So propranolol also has a long-term effect on the fear response.'

I get an association with the controversial obedience study by Stanley Milgram.

'The Institutional Review Board approved our research in advance. The subjects received an unpleasant electrical shock, but it could not be painful.'

Could you really say that actual fear was involved?

'Hard to say. Laboratory studies can't be compared to daily life. Many PTSD patients have lived through very bad experiences.'

The research is promising for future fear treatment methods. What is missing in the current treatment methods?

'Common therapies work through extinction: patients are repeatedly exposed to fear-inducing stimuli, gradually weakening their fear response. This is because during treatment they experience again and again that there is no reason to be afraid. These treatments are reasonably effective, but research shows that the fear response can return. With propranolol we can permanently erase the emotional brain, in which fear memories are stored.'

Was the research cause for a lot of discussion?

'After the first paper, we got a lot of media attention, both positive and negative. Some people were afraid that by erasing the emotional brain you would not only lose the fear response but also the declarative memory—the stored knowledge about the fearful experience. But the memory stays. It's just the emotional charge that extinguishes.'

LABORATORY STUDIES CAN'T BE COMPARED TO DAILY LIFE

Why is that important?

'When people live through a bad experience, they want to learn from it so they don't end up in the same situation again. When you've been bitten by a dog, you want to stay away from it. In that situation, it's important to remember that mean dogs exist, too.'

Drugs don't differentiate between wanted and unwanted emotional memories.' When I see a photo of my deceased grandpa after taking propranolol, will I have lost the positive feelings associated with that memory, too?

'There are many conditions that need to be met before propranolol will work on the emotional brain. It's important, for example, to correctly reactivate fear memories—that's not a given. What's more, thousands of people take propranolol for high blood pressure and heart conditions. They, too, still have their positive memories.'

How does propranolol work?

'We suspect that the substance blocks the protein synthesis necessary for memory reconsolidation. Reconsolidation is the process during which the activated memory is stored again. Propranolol disturbs this process, and in such a way that the emotional memory trace is no longer filed away as fearful, and there is no fear response.'

What is it like to work on this for four years?

'Very interesting. It's fascinating that a seemingly small manipulation has so much effect and can have all sorts of implications for treatment in the future'

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Marieke Soeter

THE NEUROCOGNITIVE SECRET OF IMPULSIVITY

by Dagmar van der Neut

Impulsivity and decision-making, those are the main themes of an ambitious research project that will be conducted within the university research priority program Brain & Cognition and that stretches across research groups from different faculties at the University of Amsterdam and beyond. Philosophy, biology, economics, psychiatry, genetics, electrophysiology, neuropharmacology, mathematics and psychology—all those disciplines come together in one large research project: Decision-making and adaptive control over impulsive actions. The goal: to understand the neurocognitive mechanisms behind decision-making, and particularly those behind impulsive decisions and actions.

DIMENSIONS, NOT DISORDERS

Richard Ridderinkhof, Eric-Jan Wagenmakers and Birte Forstmann are the lead researchers in the Faculty of Psychology. Together with Frans van Winden, professor of economics, and Damiaan Denys, professor of psychiatry at the AMC, they supervise postdocs and graduate students who will conduct seven different research projects.

This interdisciplinarity has added value, says professor of developmental psychology Richard Ridderinkhof. 'In all those disciplines, we've already been working on specific research questions for some time. But what is sometimes lacking are a number of approaches or handles that would enable us to study decision-making and impulsivity in all its richness.'

Economists, for instance, will approach psychologists and neuroscientists for collaboration, says professor of economics Frans van Winden. 'Economic decisions turn out to be influenced by various social, affective and cognitive processes. Out of these collaborations new disciplines arise, such as neuroeconomics.'

The collaboration between disciplines and the elimination of boundaries between them also fits with a shift in opinion about psychic disorders. Ridderinkhof: 'In the past, we thought in terms of separate disorders. Now we're starting to think in terms of dimensions and concepts that go across disorders. Impulsivity is such a dimension. You see disruptions of it in Parkinson's Disease, ADHD, Obsessive Compulsive Disorder, addiction, eating disorders and aging.'

WHAT'S GOING ON IN THE BRAIN?

In the brain, it appears that it's mostly the frontostriatal circuit that regulates impulsivity and control over impulses. That circuit consists of the striatum—a structure situated somewhat deeper in the frontal lobe—and the prefrontal cortex. Ridderinkhof: 'While driving, most actions are done on automatic pilot. The striatum plays an important role in this. But when you approach a roundabout, sometimes some actions have to be temporarily stopped until it's clear what you have to do. Do you have the right of way, or not? Which exit should you take? Which lane should you get into? Should you downshift? Order is required for those actions. The frontal cortex then joins in to adjust the automatic actions and set priorities.'

In impulse control disorders, it is possible that the striatum responds too quickly to a first impulse, or that the frontal cortex cannot sufficiently adjust. For patient treatment, it is crucial to know what exactly happens in the brain. Because where should you intervene?

In serious cases of Parkinson's and OCD, physicians are already using Deep Brain Stimulation (DBS). This involves, for example, intervening in the striatum, which is suspected to be hyperactive in OCD. An electrode planted in the brain core then has to reduce or shut down that activity. The function of the frontal cortex—the top-down control—can also be addressed through cognitive training, for instance. In years to come, this training will also be studied as part of this project.

Ridderinkhof: 'You can practice flexibility, for example—not panicking when the speed of a task is being increased. But the working memory—important for top-down control of fundamental processes—or the suppressing of impulses can also be trained. For people with impulsivity problems this may be difficult, but not impossible. Brain training has been successful, for example in children with a mild cognitive impairment.'

IN THE PAST, WE THOUGHT IN TERMS OF SEPARATE DISORDERS

MOVING DOTS

To better map out cognitive and neural processes, Ridderinkhof wants to study choice processes in their most fundamental form. He and his colleagues do this by using the moving dots task, among others. In this task, a subject has to choose in which direction the most dots are moving across a computer screen. Sometimes that's easy (80 percent of the dots moves toward the right), but sometimes there is a lot of "noise" (60 percent moves toward the right, 40 percent moves randomly).

This task is a simplistic representation of the bombardment of visual stimuli that is launched at us in real life. How do we choose what is important to us in our environment? What draws our attention? How important are our intentions in what we perceive? Eventually it could turn out that someone who makes impulsive decisions too often will respond differently to such moving dots than a healthy subject.

Ridderinkhof: 'When you're impulsive, you may go for the first source of information you see. Or for the strongest, and you're not capable of "parking" that information until you've absorbed all the input. When you're waiting for a traffic light and the traffic light next to you turns green, you sometimes have a tendency start driving, too. One person suppresses this with more difficulty than another. In disorders such a dominant stimulus can be very specific—to a germaphobe (someone obsessed with cleanliness), a "dirty" door knob will be the only thing he or she pays attention to.'

The outcomes of these fundamental experiments are analyzed with mathematical models. Mathematical psychologist Eric-Jan Wagenmakers and cognitive neuroscientist Birte Forstmann play an important role in this. Wagenmakers: 'From those fundamental decision experiments, such as the dot task, you get a lot of data that is difficult to interpret. If someone is slow at deciding, for instance, you don't yet know if that's because he or she is not that good at performing the task or is being cautious and doesn't want to make mistakes. A mathematical model can clarify for each individual how cautious that person is, for example.'

'Once we've used the model to reduce the complex behavior of people down to easily interpretable psychological processes, we can link those to brain imaging data. With this type of analysis, we can identify very precisely the brain areas that are involved in psychological processes such as cautiousness.'

Neuroscientist Birte Forstmann can make visible the brain cores and neural networks involved in decisions in every individual subject. Forstmann: 'Using ultrahigh-resolution scanners, a fairly new technique, we can zoom in on very specific brain areas that are deep inside the brain and very small. And diffusion weighted imaging makes visible the white matter tracks, the highways of the brain. We have preliminary evidence that there is not only a difference in brain activity between cautious and fast decision makers, but that the brain structures are different, too.'

THE ELDERLY PERSON DOES NOT EXIST

Although there will be a lot of focus on studying the fundamental underlying processes present in every human, Ridderinkhof also wants to study individual differences. This, too, is a new trend in the cognitive neurosciences.

Ridderinkhof: 'In the past, these individual differences within certain groups—such as the elderly—were seen as noise. But now we actually use those differences to get a better view of the nature of underlying processes. When you look at cognitive flexibility, elderly people turn out to be less flexible than young people, on average. But elderly people differ more from each other than younger people do! A 90-year-old is sometimes as flexible as an average forty-year-old, and there are young people who are as rigid as the average senior. We simply cannot talk about the elderly person.'

It is interesting to find out what causes these differences, says Ridderinkhof. 'Because not every addict responds equally well to a particular treatment, for example. We know far too little about this. That's why this project is so important.'

UNIQUE OPPORTUNITY

Also new in this project is the use of combinations of different measurement techniques, such as fMRI, EEG, TMS and DBS. In the past, these techniques were predominantly used by themselves. But now, for example, an EEG will also be recorded while a Transcranial Magnetic Stimulation (TMS) treatment is being performed. That shows the direct effect of the stimulation on the brain. It also allows—much more clearly than before— mapping when and how different brain areas communicate with each other.

'THIS HAPPENS NOWHERE ELSE IN THE WORLD'

The collaboration between the different disciplines also facilitates research that would not have been possible within the researchers' own faculty. For example, in collaboration with the AMC and the Faculty of Economy a study is now running that examines the taking of financially risky decisions. Patients with a severe form of compulsive disorder, depression and addiction are being treated with Deep Brain Stimulation (DBS) at the AMC.

Damiaan Denys, professor of psychiatry at the AMC: 'In these patients, two electrodes are planted deep inside the brain's reward center. These allow us to correct the activity in the brain circuits. But you can also connect the electrodes to EEG equipment and use them to conduct measurements. The patient can then perform cognitive decision tasks, and we can simultaneously see what exactly happens in the brain. In this way, we obtain very special information, such as how the brain responds to reward and punishment or what happens in the reward center when someone takes risky decisions. It is the first time that this is being studied in this way. That happens nowhere else in the world.'

These types of experiments will certainly result in joint publications in years to come. Ridderinkhof especially hopes that the project will lead to progressive insight. 'I don't have the illusion that in a few years we'll know everything exactly. But given the multidisciplinary and multimodal approach I expect that we'll be able to make considerably large strides.'

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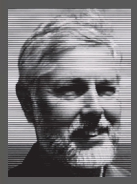
Frans van Winden


Richard Ridderinkhof

At the neural frontier of conscious and automatic control

by Dagmar van der Neut

This summer, Sanne de Wit of the developmental psychology program group will start her postdoctoral research into the cognitive and neural mechanisms that are at the foundation of impulsive actions, one of the projects within the university research priority program Brain & Cognition. De Wit will follow up on the doctoral and postdoctoral research she previously did—at the University of Cambridge and for the past two years at the Acacialab of Richard Ridderinkhof—into the role of fundamental learning mechanisms in functional and dysfunctional behavior such as in Parkinson's Disease, obsessive-compulsive disorder (OCD), addiction and obesity.

De Wit: 'Every human has two types of control over his or her behavior: targeted, conscious control and automatic control. Targeted control is more flexible, but automatic control is important, too. Driving a car is a common example. If you haven't been doing that for very long, you'll need a lot of focus with each action and will use targeted control. An experienced driver handles almost everything automatically and without mental effort. Both mechanisms are important for survival, but things can also go wrong. I will study the neural basis of the balance between these two types of control, and potential disruptions of this balance in, for instance, addictions, OCD or cognitive aging.'

What can go wrong in these control systems?

'Disrupted targeted control can lead to difficulty controlling or suppressing impulses. When the habit system is out of balance, people can be more sensitive to external stimuli. Some compulsive patients "have to" act out certain ritual behaviors, for example. These habits have grown so strong that the automatic system takes over, as it were. When the balance between the two systems has been disrupted, they can also strengthen each other. An alcoholic, for instance, is already very sensitive to the stimuli that provoke alcohol consumption, but the effects of the alcohol reduce the targeted control, which makes the automatic process even more dominant. This can cause someone to end up in a downward spiral.'

Young people, elderly people, children, patients with obsessive-compulsive disorder; you're going to study quite a few groups. Do you expect to see similarities or, rather, difficulties?

'The idea is that all those groups share common underlying neural mechanisms. But I do expect to see group differences. In some elderly people, there are indications that the control system works less well. In Parkinson's disease, the reverse appears to be true: these patients will more likely experience problems forming habits. Their behavior becomes laborious and slow, and they increasingly have to put in much mental effort. The same neural systems are being influenced, but in a different way. It's especially interesting to compare those various groups and look at individual differences.'

How will you study this?

'I use very fundamental conditioning experiments. In collaboration with my colleagues Richard Ridderinkhof and Reinout Wiers, I recently studied children with obesity. We found evidence that they were strongly influenced by external stimuli that made them think about unhealthy snacks at a subconscious level. When a neutral visual stimulus—in this case a Chinese symbol on a computer screen—had been connected to chocolate, for example, the subjects later subconsciously chose—upon seeing that symbol—much more often for an action that led to receiving chocolate rather than cucumber. Even though they indicated they liked both equally well. In these children, automatic control appears to be out of balance. More and more, we see how powerful these types of simple learning mechanisms are. They can be at the basis of dysfunctional or unwanted behavior. Smokers, for example, will find

it much easier to quit if they move and leave their familiar environment. It's these mechanisms that hide behind that. They can then avoid the external stimuli that have a strong association with their addiction. That's why after rehabilitation, drug addicts are discouraged from going back to their old, familiar user locations.'

How are you going to relate this to brain processes?

'Sometimes people do cognitive tests while they're in an fMRI scanner, for instance. We can then see whether impulsivity is indeed connected to decreased activity in, for example, the prefrontal cortex. But we also want to start studying whether we can predict how targeted someone is based on individual differences in brain structure and brain networks. One way we can do this is through scans that show the differences in brain structure. In combination with research into differences in genetic makeup for dopamine production we can eventually get a complete picture of how vulnerability for such conditions as addiction or OCD arises.'

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Sanne de Wit

SOME COMPULSIVE PATIENTS *HAVE TO* ACT OUT CERTAIN RITUAL BEHAVIORS

THE ROLE OF NEURAL PLASTICITY IN CONSCIOUS PERCEPTION

IN SEARCH OF CONSCIOUSNESS IN THE BRAIN

by Ger Post

For thousands of years, humans have tried to come to a definition of consciousness—in vain, say professor Victor Lamme and his colleagues. They want to explain conscious perception from an entirely different angle: from the cells in the brain. The neurobiological answer to the question of what exactly is consciousness usually comes down to the fact that consciousness somehow occurs through the interplay between different brain areas. In other words, consciousness depends on a complicated communication between areas that meld together information about various characteristics of an object into a whole: the scene you observe or the object you see. Thus far, research has focused primarily on finding brain areas that become more active when someone perceives something consciously, with the associative parts of the cortex as the usual suspects.

PLASTICITY

With the project, 'The role of neural plasticity in conscious perception,' one of four projects awarded within the university research priority program Brain & Cognition, Lamme of the Faculty of Social and Behavioural Sciences (FMG) and his colleagues from the Faculties of Science (FNWI) and Humanities (FGW) want to approach consciousness from a different angle. According to the researchers, the key to consciousness lies in the way neurons change their mutual connections, so-called plasticity. 'We want to prove that the way in which we consciously perceive visual pictures or sound depends mostly on how perception causes changes in the wiring of the brain,' the scientists write in their research proposal.

Using a series of experiments they want to test this hypothesis. First and foremost, the research focuses on the connections between neurons, following up on earlier research conducted by Lamme. The latter showed that a visual signal can be unconsciously processed within a hundred milliseconds. Someone can respond to this information, for example by catching a ball in a reflex, but it's not until after that—when higher and lower-level areas of the brain give each other feedback—that a conscious picture of catching the ball is formed. Now the expectation is that during this unconscious, rapid brain activity the wiring of the brain remains unaltered, while these neuronal connections do change during conscious feedback interactions.

A logical consequence of this expectation is that if these changes in neuronal connections (plasticity) can be blocked, this does not influence unconscious processes, but it does affect the necessary interactions for consciousness. Anouk van Loon will research this in humans. Cyriel Pennartz's group will look into this same question in rats.

Pennartz: 'We will test this in rats by looking at whether their visual perception changes when we administer locally into the visual part of the cortex a pharmacological substance that blocks plasticity and a strong activation of neurons. This is how we'll study whether this so-called NMDA-receptor induces a so-called blind-sight effect. That is, whether rats still show an automatic behavioral response to a visual stimulus, but also—through their behavior—illustrate that they haven't seen this stimulus.'

If the researchers do find that blocking plasticity primarily influences conscious processes, this would yield, according to Pennartz, a radical new insight into how consciousness works and how it comes about. 'One school of cognitive neuroscientists, for example, poses that consciousness comes about through the activation of networks in the higher associative regions of the cortex, which is also referred to as the workspace hypothesis. A confirmation of our hypothesis would shift the attention to the interaction between higher and lower visual areas in the cortex.'

HOW DO I KNOW IF BRAIN ACTIVITY SIGNALS CONSCIOUSNESS OR JUST UNCONSCIOUS PROCESSING?

EPIPHENOMENON

A subsequent question the researchers want to answer: does learning require consciousness? Lamme and his colleagues think so and believe there is no such thing as unconscious learning. Aren't they neglecting piles of research that shows that people can be guided by unconscious stimuli—and actually learn things? No, say the researchers, because this unconscious guiding (priming) lasts only a short time and there is no solid evidence that such primes have any effect in the long term. Lamme: 'When you carefully weed through the literature on unconscious learning, it turns out that all forms of "implicit learning" are in fact forms of learning without attention, but not without consciousness.'

In other words, the researchers see consciousness as an epiphenomenon of memory forming. This assumption appears to contradict findings from research involving Henry Molaison. This patient—known in the literature as H.M.—died a year and a half ago. His hippocampus, an area that is important for storing memories, had been removed. Because of this, Molaison couldn't remember new experiences, but he was in fact aware of what was happening around him. Pennartz: 'Our proposal doesn't focus on the hippocampus. Our hypothesis that consciousness arises from synaptic plasticity applies to the neocortex. It revolves around the fact that, in conscious perception, feedback from higher areas of the cortex to the primary visual cortex goes hand in hand with the changing of connections. This could have very well been the case with H.M.'

Lamme adds: 'It's about memory forming in the most general, biological sense. The hypothesis is: as soon as something changes in your brain, there's consciousness. In no way does this mean that you will explicitly remember this later on. Episodic memory is nothing but a very specific—and rather mysterious—form of memory.'

Whether learning necessarily goes along with consciousness—and not with attention—is the subject of a subproject by musicologist Henkjan Honing. Although all other subprojects focus on visual perception, Honing and his colleagues will focus on processing musical rhythms. In earlier experiments they found that a sense of rhythm appears to be ingrained in humans. Newborns, for example, already appeared to have a sense of rhythm.

'In a series of listening experiments with non-musicians we also found that their rhythmic expectations were being processed even if they focused their attention on something else, for example when they were watching a video with subtitles,' Honing says. 'In the planned experiments we will examine how open this rhythmic perception is to learning and to what extent attention or consciousness guides this.'

FARMERS AND OFFICE CLERKS

Lastly, research is planned into how visual perception is determined by similarities in the images we see daily. The idea is that our neural system has adapted to (hidden) statistical regularities in images of our environment, such as fields and forests. Lamme: 'Even though all those images seem extremely different, they do display a hidden similarity in the way contrast is divided. We've discovered that our brain has adapted to this through learning, or perhaps even as part of evolution. So what has been ingrained by our experiences determines our conscious perception.'

People with different professions will participate in this research. In this way, they will test, for example, whether farmers learn outside scenes in a different way than office clerks who are inside all day. They'll also look to see whether people with indoor or outdoor jobs react differently to artificial images that have the same hidden contrast patterns as outside scenes. The expectation is that farmers are better at perceptual tasks in which they have to detect small hidden objects in a picture, for example, and show an elevated neural activity for artificial scenes with the same statistical regularities.

Arnold Smeulders from FNWI will join Sennay Ghebreab from FMG in conducting research into these "hidden" statistical regularities. Ghebreab explains: 'If our expectations come true, this could mean that people can differentiate in a single glance an image of a beach from one of a street, because they react to the differences in global statistic regularities in these images. If we can prove that these statistical regularities provide for a conscious perception in our daily lives, this would mean that the current theories on attention and how we detect objects or navigate spatially must be reconsidered. Because those theories are all based on the assumption that consciousness arises from a bottom-up integration of parts of a picture—that an object is formed from various characteristics, and that these objects are subsequently being forged into scenes.'

COMA

A neural definition of consciousness would provide a lot of answers to questions that are still open right now, according to Lamme. 'You can then objectively determine whether there is consciousness in all those cases we've been wondering about for years. For example, in patients who are in a coma or a vegetative state. Wouldn't it be fantastic if you could determine whether someone who is in a vegetative state has conscious sensations of voices around him, or of the people who touch him? Until not so very long ago, a doctor would peer deep into the eyes of such a patient and would tell the family: "The lights are really off here."'

Now, brain scans are being done around the world, and patients who look unconscious from the outside are found to show enormous differences in brain activity, Lamme knows. 'Some brains do react to voices; others don't. Some patients even react to directions such as "imagine walking through the room." You then see the same brain activity as in someone who is awake and is given the same direction. The key question related to those measurements is, of course: how do I know if brain activity signals consciousness or just unconscious processing? Such a neural definition would be the solution for that.'

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http://staff.science.uva.nl/~ghebreab/
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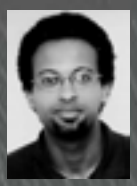
http://home.medewerker.uva.nl/a.m.vanloon/


Cyriel Pennartz


Henkjan Honing


Sennay Ghebreab


Victor Lamme

THE LIGHTS ARE REALLY OFF HERE

When do you see something consciously?

by Ger Post

Anouk van Loon, an employee of the Department of Psychology, studies the relationship between consciousness and brain activity in the visual cortex. Just before getting on a plane to the United States to present her results at a conference there, she talks about her doctoral research.

How did you get involved in this project?

'I found all the psychology courses to be rather boring with a lot of open doors, until I attended classes taught by Victor Lamme in my third year. I immediately thought it was great. Consciousness is something that has kept people busy for ages, and now the cognitive neurosciences can help us understand it. What's also nice is that our group uses every imaginable technique, from fMRI to EEG to pharmacology, which now occupies me.'

Which question are you trying to answer?

'My research is part of Lamme's efforts to come to a neural definition of consciousness. Rather than coming up with a theory and then going back in the brain, which is now common in psychology and philosophy, we first look at the activity in the brain and relate that to consciousness later on. We focus particularly on visual processing, since a lot is known about its neural background.'

Can you give an example?

'When processing a picture, for instance, you can differentiate between two processes. First, there's a wave of activity of the lower-level visual areas, which for example respond to the details in a picture, to the higher-level visual areas, which respond to larger fields. Within 100 milliseconds all the information in the picture shoots through the entire brain, but that does not yet mean there's consciousness. That only happens with recurrent interactions, when the higher-level and lower-level areas give each other feedback. A neuron that responds to the detail in a picture does not yet know what it's a part of. The neuron only knows that when it receives information from a higher-level area that tells it that it's part of a figure in the foreground and thus has to be more active. It's not until these recurrent interactions that people see the picture. Now, of course, the question is: what makes these recurrent interactions so special compared with that first wave of brain activity? My role in this project is to look at the neural mechanisms behind the later interactions. I do this by influencing these processes through pharmacology.'

How do you use drugs to influence these interactions?

'Neurons communicate with each other through substances, so-called neurotransmitters. It turns out that with drugs we can ensure that the brain activity of subjects is normal during the first wave of activity, but that activity decreases during the interactions. You also see that the drug causes people to have difficulty differentiating a figure from its background. Instead of shutting down the entire brain, this drug has a specific effect on the activity of neurons during recurrent interactions.'

According to the project description, plasticity—which involves changes in connections between neurons—is essential for consciousness. Do your results illustrate this?

'That isn't clear yet. We see the effect on recurrent interactions when we influence the neurotransmitter GABA with drugs. In some studies, this substance has been tied to changes between neuronal connections, but this is still being disputed in the literature. The neurotransmitter glutamate has more often been shown to play an important role in plasticity. But when we used a drug that inhibits this neurotransmitter we didn't find any effect.'

Do you have an explanation for this difference in results?

'I think it's because we used a weak drug to inhibit glutamate transfer. The drug I used is also an ingredient in cough syrups, for example. I will be doing a similar task in a follow-up study, but in combination with the anesthetic ketamine. That affects the same process as the cough syrup, but is a stronger drug. With this drug, I do expect to find an effect on recurrent interactions. Right now, it's too early to say with certainty that the drugs influence plasticity.'

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Anouk van Loon

WHAT MAKES THESE RECURRENT INTERACTIONS SO SPECIAL?

SEARCHING FOR THE BASIS OF CATEGORIZATION

by Vittorio Busato

'How do babies who don't yet speak a language learn to differentiate between types of categories such as dogs and cats; between sounds and speech sounds such as ba and da or p, d and g; between primary emotions such as angry and happy, safe and unsafe? How are such categories represented in the brain? How do babies generalize knowledge they acquire to other categories? Is there overlap in that learning process? What do children learn from feedback about mistakes made? How do these young children make a developmental leap and suddenly acquire the insight to accurately differentiate between categories? What are the characteristics of those categories that have emerged? Does categorical perception take place, or would we rather speak of a continuous perception based on which a child comes to a categorical classification? What about the individual differences between babies in the speed at which they familiarize themselves with a categorization process? These are all important questions that are at the basis of how we learn to make various types of differentiations in the world around us.'

These are the words of Maartje Raijmakers. She is an associate professor with the Department of Psychology at the University of Amsterdam (UvA). Together with Paul Boersma and Susan Bögels, professor of phonetics and professor of orthopedagogics at the same university, respectively, she is responsible as the lead researcher for the project Models and tests of early category formation: interactions between cognitive, emotional and neural mechanisms, one of four projects awarded in the interdisciplinary and interfaculty university research priority program Brain & Cognition of the UvA.

NEW MODEL

All three are among the few researchers at the UvA who already do scientific research with babies and test them here, too. What's more, Raijmakers and Boersma have substantial experience in modeling these types of categorization processes and have published on this. Raijmakers has developed the adaptive resonance model for category learning, a model that—briefly put—tries to explain how feedback helps children to differentiate between categories. Boersma is the spiritual father of the so-called bidirectional multi-level language acquisition model, a model that describes how we acquire a language through listening and speaking. What exactly it will look like they don't yet know in this phase of the project, but based on experiments Raijmakers and Boersma hope to eventually combine their two models into a new model.

In this recently started project they not only unite practical knowledge they gained while conducting baby research, but also their expertise in the area of phonetics, psychology and pedagogy with respect to learning and forming categories. Especially for this project a new baby lab will be set up, complete with state-of-the-art equipment to register eye movement in babies and record EEGs, among others.

Paola Escudero Neyra, who is involved with this university research priority program as a postdoc, has gained some experience recording EEGs in babies and has completed several exploratory studies at the baby lab of American Scott P. Johnson in Los Angeles. Johnson, an internationally renowned expert in the area of cognitive neuroscientific baby research, will be involved in this project as a visiting professor at a later stage. Together with their postdocs, graduate students and undergraduate students, Raijmakers, Boersma and Bögels hope to find, as part of this extensive research project, answers to fundamental questions about the inception and forming of categories. As an added practical advantage, they will be able to join efforts to recruit babies for their experiments.

Bögels thinks that with this project they have started a rather unique interdisciplinary collaboration, from an international perspective. 'My research is predominantly focused on the origin of fears and the specific role of parents in this—social referencing is the scientific jargon. There are evolutionary aspects to primary emotions such as fear and anger, but we also partly learn those through parents and other experts. Parents will send signals as to whether something is safe or not. Babies learn to classify those stimuli in categories such as safe or dangerous and will base their behavior on those: proceed or avoid. The added value of our collaboration that I'm most looking for is that we will discover more about the possible overlap in learning different types of categories. By bundling our knowledge and expertise we will be able to fine tune these processes much more in terms of methodology.

Boersma has a similar opinion. 'Although our project involves basic science research, part of it could most certainly be characterized as exploratory. That's why, frankly speaking, I don't have very concrete expectations, other than that as researchers from different disciplines we will certainly learn a lot from each other.'

AS RESEARCHERS FROM DIFFERENT DISCIPLINES WE WILL CERTAINLY LEARN A LOT FROM EACH OTHER.

NEW PARADIGM

The usual paradigm to study category learning in babies is the so-called habituation paradigm. Babies will repeatedly get to see pictures of one type of category, such as dogs, or they will keep hearing a similar sound, such as ba. At some point babies will start to find that boring. They'll get used to those similar stimuli and will therefore likely recognize them; they've learned something. They will barely pay attention to a new dog, but they will when they see a picture of a cat or hear a different sound. Research shows that this shift in attention can be seen not only at the level of behavior, but also in the brain activity of babies.

'We're not only interested in whether a baby learns something but particularly in how he or she learns something,' Raijmakers says, after explaining the habituation paradigm. But this requires a different paradigm that is closer to how adults learn to categorize. 'We will study, among other things, how children learn two categories at the same time,'Raijmakers continues. 'We have developed a task in which babies get to see moving dogs or cats on a screen. The dogs briefly disappear from the screen and reappear on the right side, while the cats reappear on the left side. During this task we will track the eye movements of the baby and will figure out whether a baby learns to anticipate where cats or dogs will reappear. When a baby correctly predicts this, as indicated by the eye movements, he or she has learned something about the categorization. Subsequently, you can use new pictures to test whether the baby can generalize this categorization. So we're looking at predictive ability; we don't settle for an observation of whether or not a child is bored.'

Another technique researchers will use is the so-called morphing of photos and sounds. Using special software, photos of facial expressions can slowly transition from angry to happy, for example. A program developed by Boersma can very gradually morph artificially generated sounds into one another. Bögels: 'This technology enables us to zoom in much more precisely on the attention- and categorization process of babies and any shifts in that process.'

PSYCHOEDUCATION

All in all it's an ambitious and interdisciplinary research project that Raijmakers, Boersma and Bögels are planning. Nevertheless the three scientists are cautious not to have exaggerated expectations of what the project will eventually yield, especially because of the exploratory aspects of their research. Boersma hopes that they will at least come to a new model of how the brain learns to categorize and classify. 'Those processes, in my view, are in large part symbolic for what makes us human. And perhaps it will yield applied knowledge that will eventually benefit dyslectics, who have trouble forming sound categories, or autistic children, who have trouble reading emotions on faces."

Bögels expects that their fundamental research will yield practical knowledge on the learning and unlearning of fears in young children as part of interactions with their parents. 'If our research project yields new implications on this, that's important for psychoeducation on the origin and treatment of fears. It's important for us to teach parents how they can think about certain fears in a more nuanced way, but especially how they can impart that on their children.'

Raijmakers is mainly focusing her hopes on better theory development on how we learn to categorize. 'We won't stop at descriptions, but will try to come to explanations. How, for example, does a baby determine whether an unexpected event means danger or is interesting to explore? When we understand more about the developmental process of early category formation, we also learn to better understand the functioning of adults.'

http://mraijmakers.socsci.uva.nl/
http://www.fon.hum.uva.nl/paul/
http://home.medewerker.uva.nl/s.m.bogels/
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Maartje Raijmakers


Paul Boersma


Susan Bögels

WE'RE NOT ONLY INTERESTED IN WHETHER A BABY LEARNS SOMETHING, BUT PARTICULARLY IN HOW HE OR SHE LEARNS SOMETHING.

A fascination for how babies learn to classify the world

by Vittorio Busato

Paola Escudero studied linguistics in her hometown of Lima and applied linguistics in Edinburgh. In 2005 she earned her PhD at the University of Utrecht based on her dissertation "Linguistic perception and second language acquisition: Explaining the acquisition of optimal phonological categorization." Since 2000, she has worked with Paul Boersma, professor of phonetics at the Humanities Faculty of the University of Amsterdam (UvA) who was also one of her promotors.

Escudero is initiator of the priority program project Models and tests of early category information: interactions between cognitive, emotional and neural mechanisms. As a senior postdoc, she will be jointly responsible—with postdoc Dorothy Mandell—for a new baby lab and the experiments that will be conducted there as part of this project. Recently, Escudero conducted some exploratory studies at the lab of Scott P. Johnson in Los Angeles and gained experience recording EEGs in babies, as well as registering their eye movements.

How did you, as a linguist, become involved in this transdisciplinary research?

'I have always been fascinated by how people classify the world around them. Initially, as a linguist, I focused on categorizing speech. This research project enables me to explore for the first time how young children learn to classify auditory, visual and emotional information. Now that I have more knowledge of the psychological literature on categorization, I can't just think in terms of one modality—speech, in my case. That's why, when the research priority program Brain & Cognition presented itself, I approached both Maartje Raijmakers and Susan Bögels to participate in this project, along with Paul Boersma.'

How difficult is it to do scientific research with babies?

'Babies enjoy looking at new things, but they also get bored easily. You have much less time to do research with babies, so experiments should be short and fun. In our upcoming study, it doesn't matter that much how long babies focus on a particular task. The most important thing is that they don't get confused from the moment the experiment starts. Some babies just don't feel like participating, either because they're tired or don't want to look at a computer screen. However, most babies are interested, but gradually lose their interest. Some babies just have a longer attention span than others. In our experiments, we register that through their eye movements, independent of how much time they spend on a task.'

Is recording EEGs in babies that simple?

'Experience tells us that if we play with the baby before applying the electrode cap, registering their brain activity is a lot easier. Babies have to feel at ease—that's crucial. Some babies try to remove the cap; others barely seem to notice that they're wearing it. You can't predict which babies will or won't participate. That's why we try to test as many as we can. EEG data of babies needs to be analyzed in a slightly different way than that of adults, but the data on visual categorization that I analyzed in the United States shows the same patterns as in adults.'

IT IS CRUCIAL THAT BABIES FEEL AT EASE

What is known about categorization from brain research in babies?

'Very little research has been done in that area. What's more, these studies used different ways to measure brain activity. For example, it is known that in babies, new objects, faces and memories lead to an increase in brain activity. You can also see a difference in brain activity when children look at new pictures or objects that belong to the same category; it is lower than with pictures or objects from a different category. This type of research used very simple objects and categories. Most studies focused predominantly on so-called event-related potentials that have to do with attention, and not on other components of brain waves. In our project, on the other hand, we will explore new methods of analysis for brain activity and new types of stimuli for the three domains.'

Using free association: what do you think your research will yield?

'In about five years I hope we will have found an answer to the question of how early categorization takes place in the visual, auditory and emotional domain and what the commonalities are. And to me personally it's very important that we will try to explain the underlying mechanisms.'

http://www.fon.hum.uva.nl/paola/
http://www.hoelerenbabies.nl
http://www.babylab.ucla.edu/index.php?page=publications

Paola Escudero

Agenda

BRAIN & COGNITION LECTURES

2010

SEPTEMBER 14
OPENING
BRAIN & COGNITION

SEPTEMBER 22
HANS VAN DONGEN

OCTOBER 20
EDVARD MOSER

NOVEMBER 17
MARK BOUTON

DECEMBER 15
TO BE ANNOUNCED

2011

JANUARY 26
TO BE ANNOUNCED

FEBRUARY 23
TO BE ANNOUNCED

MARCH 23
ANIL SETH

APRIL 20
ROGER RATCLIFF

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