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25 February 2011

Donders Institute
for Brain, Cognition and Behaviour
Newsletter

The Donders Newsletter is published three times a year by the Donders Institute for Brain, Cognition and Behaviour, which consists of research groups at Radboud University Nijmegen and the Radboud University Nijmegen Medical Centre as well as the Max Planck Institute for Psycholinguistics. Its purpose is to keep you informed of developments and important news in the field of neuroscience.

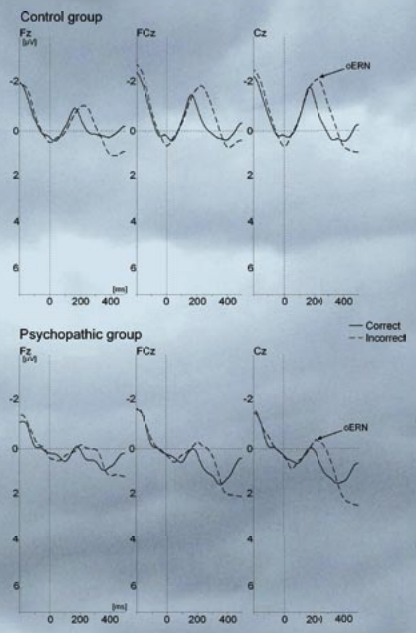
In the autumn of last year the Donders Institute (DI) had its first evaluation, with a committee of reputable scientists looking at our scientific performance, our organisation and our prospects. This resulted in a series of very useful suggestions that will be implemented over the coming year. We will continue working on strengthening our governance structure, improving the coherence of our research portfolio with its four themes, and clarifying and improving the career paths we offer. The proposals of the current Dutch government are – to put it mildly – not helpful for securing our scientific future. We will need even more creativity and flexibility than we had in the past to sail through this period. Transparency and flexibility will therefore be crucial during my period as Chairman of the Board of Directors. But, with the amazing potential of intellect and creativity that the DI has on offer, I am confident that, even with these clouds over our heads, we will come out stronger.

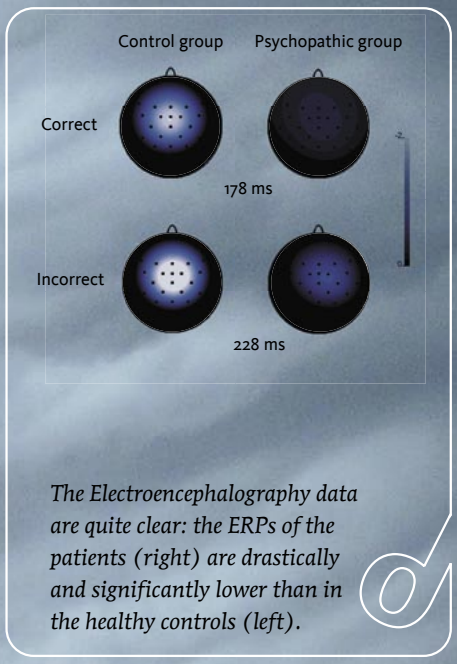
In this issue of the Newsletter you will find interviews with a cross-section of the many creative and talented people at the Donders Institute: Bert Kappen, Inti Brazil, Ard Peeters and Erik van den Boogert. I hope you enjoy reading it.

Peter Hagoort

Radboud University Nijmegen

www.ru.nl/donders





The Electroencephalography data are quite clear: the ERPs of the patients (right) are drastically and significantly lower than in the healthy controls (left).

Psychopaths

Insensitive to the behaviour of others – good or bad

Until recently, little has been known about the psychopathic brain. The purpose of a Donders initiative that spans the whole institute and involves close cooperation with a clinic for criminal offenders is to unravel the basic brain make-up associated with the affliction. Hopes are high that an effective treatment will eventually be found – or at least indications which therapies should be avoided. A recent paper in *Biological Psychiatry* explains why group therapy is not likely to fit the bill.

It wasn't exactly spelled out in the advertisement for a PhD position, nor mentioned in the first job interview at the Donders Institute. The second interview took place in the Pompe Kliniek, a high-fenced, heavily guarded clinic for criminal offenders in Nijmegen. It was only then that Inti Brazil got a clue what 'severe anti-social personality disorder' referred to. Psychopaths: dangerous people. Inti wasn't put off – he accepted the job.

He started working in the psychiatry department.In 2007 they began conducting the initial experiments which led to a first publication in 2009. After that, he successfully applied for a Mosaic grant, which enabled him to continue his research for another four years. (The NWO Mosaic programme is designed to attract more ethnic minority graduates into academic research. Inti comes from Curaçao.) Since then he's moved into Ellen de Bruijn's lab at the Centre of Cognition, where research focuses on unravelling the cognitive and neural mechanisms underlying disturbed social behaviour and adaptive control in various psychiatric disorders, including psychopathy. As a result, Inti became the embodiment of the joint Donders effort to gain more insight into psychopathy.

Personality disorder

Psychopathy is a personality disorder that's characterized by distortions in emotional processing and anti-social behaviour. Psychopathic individuals are known to show an almost total lack of empathy, guilt, or remorse, combined with anti-social behaviour fuelled by impulsivity, poor planning skills and frequently criminal intent. In clinical practice, psychopathy is considered extremely hard to treat. The anti-social lifestyle of psychopathic offenders reflects severe problems in acquiring social norms and rules, often leading to criminal behaviour. The men serving a sentence in the Pompe Kliniek have been convicted of serious offences such as murder and violent rape.

The pathological brain mechanisms underlying psychopathy have remained relatively opaque so far, says one of the initiators of the project, psychiatrist Robbert Jan Verkes. He's associated with both the Pompe Kliniek and the medical section of the Donders

'In an informal conversation people with psychopathic disorders can be very polite and, in fact, appear quite normal.'

Inti Brazil

Centre for Neuroscience. 'What is the anatomy of this disorder? And how can we treat it? We had to start with a basic understanding of the altered brain function of these men. There's growing evidence suggesting that patients with psychopathy have biological and cognitive abnormalities that seem to play a substantial role in the development of disruptive behaviour. Because of their typical inability to conform to social norms and the fact that we don't have any effective therapies, our research focuses on action monitoring and learning.'

Lab in a very special location

Inti spent his first year setting up an EEG lab in the Pompe Kliniek itself, to minimize the hassle of transporting the convicted test participants to the university. The next step was to classify the degree of psychopathology among these patients. Inti had to sit down with them and fill in long questionnaires. 'These interviews can take four, five hours,' he says.

Does he ever feel unsafe? 'No, I don't, although I'm always aware of the crimes they've committed. It's not the same to share a room with a serial rapist as it is to be with someone who's committed five murders... But, in an informal conversation, people with psychopathic disorders can be very polite and, in fact, appear quite normal. However, it doesn't take long to notice that they rarely use words that refer to their emotions.'

Error monitoring

One way of acquiring social norms and appropriate behaviour is by observing others. More specifically, we learn by monitoring other people and imitating behaviour that leads to desired outcomes, while avoiding behaviour that ends in undesirable outcomes. This suggests that we need to be susceptible to errors committed by others in order to learn appropriate behaviour ourselves. Mirror neurons in our brain are constantly active while observing others and our anterior cingulate cortex (ACC) warns us with a loud OOPS when we see others make a mistake.

Does this work the same way for people with psychopathic disorders? Nijmegen researchers have confirmed in an earlier study that their ACC does signal when they make a mistake themselves (Brazil et al., 2009).

Inti used a modified version of the arrowhead Eriksen flanker task. Participants were seated across the table facing the experimenter and asked to monitor his performance. The behavioural and electroencephalography data that was collected were quite clear: psychopathic individuals process the outcome of others' actions (in terms of correct or incorrect) quite differently. The ERPs – the electrical response of their brain to the outcome of the observed action – were drastically and significantly lower than in the healthy controls. This was not only the case when observing a mistake; monitoring others' actions didn't provoke much of reaction at all. 'We could see that the participants were paying attention to the task, though, and that their visual system was actively engaged,' Inti Brazil says.

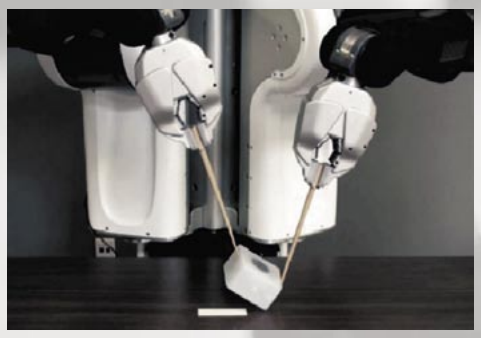
Feedback learning

'This task is fairly simple, but the implications of our findings for daily social situations, which are obviously more complex and richer in nature, might be enormous. We observe a huge number of other people's actions in our lives. So this deviation might play an important role in the acquisition of disturbed social behaviour in psychopathic offenders.'

'Together with my colleague PhD Katinka von Borries, who does the fMRI studies in this project – you can imagine the organizational worries she faces getting the detainees to the Donders lab, with two security guards in attendance – we try to find out how this afflicts the learning process. Healthy individuals learn from both positive and negative feedback, and the posterior medial frontal cortex plays a crucial role in these learning processes. Psychopaths don't respond much to punishment, but do react well to rewards... we'll see.

So far, our results indicate that group therapy is not likely to be the way to go to in treating psychopathy. This type of therapy is based on the idea that you can learn from observing others. Well, they don't.'

IR



Willow Garage's PR2 robot learns to play billiards and to manipulate chopsticks. The control methods used here, which were developed by Kappens' group, are being implemented by Stefan Schaal at the University of Southern California.

Machines – now with intelligence

In recent years there's been a silent revolution in artificial intelligence and robotics, with the application of smart statistical methods to huge amounts of data. The Intelligent Machines Symposium, which was held on 17 November in Nijmegen, provided some inspiring examples.

Over two hundred people from academia, industry and government filled the concert hall of De Vereeniging in Nijmegen. They were attending a symposium called Intelligent Machines, organized by the Foundation for Neural Networks (SNN), which brings together researchers working on artificial intelligence in the Netherlands. "The goal is to put the field better on the map here," says Bert Kappen, a professor of machine intelligence and neural networks connected to the Donders Institute. Kappen is the driving force behind the symposium. "We want to show how machine learning techniques are used in practice."

Four top international scientists gave presentations. We saw movies of fully autonomous flying mini-helicopters performing rescue operations. Intelligent, driver-less cars that quickly turn the steering wheel to avoid colliding with pedestrians who suddenly appear in front of them. And we heard about the automatic translation tools that are currently offered by the major internet search engines.

A common thread ran through the symposium: a quiet revolution based on a paradigm shift in artificial intelligence. For decades, computer scientists have tried to build intelligent computers and robots by stuffing them with pre-programmed rules – as if life was a game of chess. That led to some modest successes, but far fewer than the fathers of artificial intelligence had dreamed about in the late fifties.

The engine of this quiet revolution in recent years has been a fundamentally new approach: smart statistical methods that rapidly distil meaning from a huge mountain of data. Thanks to the worldwide web, for the first time in history, vast amounts of data are freely available: text, images and sound recordings. The result has been successful machine translation, automatic speech recognition, image recognition and smart mapping of our spatial environment. The machines are not yet able to perform at a human level, but they are a lot more capable than they were a decade ago.

Of men and machines

In fact, robot designers and developers of artificial intelligence face much the same questions as neuroscientists. How does a brain – whether natural or artificial – solve problems that arise in interaction with the world around it? Issues such as perception, reasoning, language processing, speech production and how to act are relevant in both cases.

It's not therefore surprising that Kappen's research group is part of the Donders Institute. With his artificial intelligence research he aims to contribute to a better understanding of brain, cognition and behaviour. He gives three examples from his own research. First, there's the modelling of networks of neurons. "We try to understand how the changing strength of

"The basis of the quiet revolution in artificial intelligence in recent years is a fundamentally new approach: smart statistical methods that rapidly distil meaning from a huge mountain of data."

Bert Kappen

synapses affects the network behaviour of neurons. Our models describe the behaviour of some 100,000 to 1,000,000 neurons."

Kappen and his collaborators also use machine learning techniques for brain-computer interfaces, a second example. "We investigate how a subject, using his or her mind, can control a cursor on a screen. We record the thoughts of the subject – based on MEG or EEG signals – and we train a neural network to recognize patterns in these signals."

A third example lies in the field of robot motion. How does a robot know how to move its arms? A simple spray painting or welding robot in a predictable factory environment is programmed to move its arm at a certain moment in a precise way from A to B. But our everyday reality is full of unpredictability. Suddenly a cart appears. Over there a man emerges. How does a human - or artificial - brain deal with this? That's an important research question.

Kappen: "We've developed a new control theory which can help robots to learn in such unpredictable situations. The theory predicts, among other things, that the noisier the environment, the later the brain takes a decision. We've also measured this in the brains of human volunteers and we can now successfully apply this theory to robots."

Intelligent wheelchair

At the end of the symposium Professor Jaap van den Herik (Tilburg University and Leiden University) led the final discussion. "When will machines become smarter than people?" he asks in an attempt to challenge the four speakers.

None of them sees any evidence that this will be achieved any time soon – even within a few decades. As Nicholas Roy, a robot engineer at the Massachusetts Institute of Technology (MIT), one of the best artificial intelligence labs in the world, put it: "We have no experimental data that can tell us anything about the moment when robots might become smarter than people. We're engineers. Predicting the future is not what we do. We're interested in building models and machines based on what we know now."

And, referring to Ray Kurzweil's best-seller The Singularity is Near (2005) on Kurzweil's prediction that machines will become smarter than humans, Roy says: "Nobody has ever said anything meaningful about the future, except to drive up the sales of a book."

Fortunately, machines don't have to become smarter than people to be of great practical use. Roy shows a movie of an intelligent wheelchair, which can be controlled by voice. Patients with severe muscle disease can ask the wheelchair to take them to the lift or to order a pizza. The wheelchair also learns from the needs and wishes of the user.

Roy: "This work improves the quality of life of patients. They can lead more independently. At the moment the most successful commercial robots in the world is the Roomba robot vacuum cleaner, quite a simple robot. That will really change. I do not see robots becoming smarter than humans, but more and more artificial intelligence designed to help people will hit the market: in healthcare, in services, traffic and transport, and doubtless in many applications that we cannot yet imagine."

BM

Weblinks

www.snn.ru.nl/symposium-2010/
Intelligent Machines Symposium, Nijmegen, 17 November 2010

www.youtube.com/watch?v=f7oD3W1kpSI
Intelligent, voice-controlled wheelchair developed by Nicholas Roy's MIT robotics group

www.youtube.com/watch?v=8Thdf_7j4dI How a robot can learn from imitation in unpredictable situations

Prof. Peeters' inaugural lecture

'A single result is not a result'

For something as complicated as depression, fundamental insights – and new research – will have to come from the universities. The pharmaceutical industry simply won't give it priority. So Ard Peeters, a former employee of Organon, was happy to be appointed to an endowed chair ('Special Professorship') at the Donders Institute for Brain, Cognition and Behaviour. Peeters, who worked for Organon and its successor companies for 20 years, has done a great deal of research on drugs to combat depression. Animal-based models generally play an important role in such research. However, during his inaugural lecture (16 December 2010) he said that there is no animal model for depression ...

A mouse may exhibit some of the characteristics of depression – no longer appearing to enjoy life, insomnia, or fear – but it can't tell us it's feeling down and having suicidal thoughts. That presents a problem. Simply combining various animal models is an improvement in itself. Peeters has suggested combining the familiar open field test with the Porsolt forced swim test, sugar water preference test, marble burying test and object memory test. A drug is then considered suitable for further study only if the mouse exhibits less depression-like behaviour in a number of tests.

Ard Peeters: "This is not ideal and that's partly because we still don't really understand depression. The term is too broad; in fact, like schizophrenia, it's an umbrella term for several separate disorders, which we need to distinguish. Only then will it be possible to trace where a disorder is based in the brain. For psychotic depression – the most severe form, in which depression is accompanied by delusions – the suspected cause is stress and a dopamine problem. You could come up with a drug that will combat this, and test it with an animal model. You wouldn't have to rely on observations of the animal's behaviour; you could see quite accurately whether the affected system is functioning better." In short, instead of research based on trial and error, we could conduct hypothesis-driven research.

Peeters' Special Professorship falls under Professor Eric Roubos' research group in Cellular Animal Physiology at the Centre for Neuroscience. There he is currently investigating another subgroup of depression: mood swings in women, influenced by the hormonal fluctuations of the menstrual cycle or following menopause. This is a milder form of depression. "We already know the substances involved: they are used as contraceptives or to reduce hot flushes. Using them to combat mood swings is new. We're going to investigate whether it works. And we definitely need to go about it more rigorously than in the average university study."

Despite his enthusiasm about the fundamental insights that universities can offer to the pharmaceutical industry, Ard is very critical of the quality of academic research. "There's a huge rush to publish, tests aren't repeated often enough, control groups are often omitted, and outdated animal models are kept in use for far too long and are never questioned. I'm truly shocked; the data from the pharmaceutical industry is much more reliable. In our world, a single result is not a result." *IR*

Meanwhile at www.ru.nl/donders

Pay a regular visit to our website to keep up to date on our news and events.

Restricted diet helps reduce ADHD symptoms

A special restricted diet should be part of the standard of care for all children with attention-deficit hyperactivity disorder (ADHD), conclude Professor Jan Buitelaar, Donders Institute and Dr Lidy M. Pelsser, ADHD Research Centre, Eindhoven, Netherlands, and colleagues. In a study, published in *The Lancet* on February 5, they report that children aged from 4 to 8 and diagnosed with ADHD benefit from an elimination diet. The children showed significant improvements in their ADHD symptoms, as demonstrated by the ADHD rating scale. The oppositional defiant disorder symptoms, which were also present in half of the children, also decreased.

Wave of death signals time of death

Donders researchers Tineke van Rijn and Ton Coenen have found an EEG signal that marks the end of life. Studying the effects of decapitating rats they observed a high amplitude slow wave after 50 seconds (awake group) or 80 seconds (anesthetized group) following decapitation. The EEG before this wave had more power than the signal after the wave. This wave might be due to a simultaneous massive loss of membrane potentials of the neurons. Still functioning ion channels, which keep the membrane potential intact before the wave, might explain the observed power difference.

Soldiers' brains adapt to threat during mission

A study of soldiers who took part in the ISAF mission in Afghanistan between 2008 and 2010 has found that their brains adapt when they are continuously exposed to stress. According to Donders Institute researcher Guido van Wingen, the perceived threat appears to be the major predictor of brain adaptation, rather than the actual events. In other words, if a roadside bomb goes off right in front of you, the degree to which you perceive this as threatening is what counts. This is what determines how the brain and the stress system adapt. These results were published in the scientific journal *Molecular Psychiatry* on 19 January 2011.

Huge media response to language study

An article entitled 'Imitation Improves Language Comprehension', by Patti Adank, Peter Hagoort and Harold Bekkering, was recently published in *Psychological Science*. It received a great deal of media attention, with interviews for radio and TV in the USA, Canada, the UK, Belgium and the Netherlands, including BBC Radio and Kink FM. This study proves that vocal imitation of an unfamiliar accent improves spoken-language comprehension.

Intellectually disabled fruit flies recover memory function

An international research team led by Hans van Bokhoven and Annette Schenck has shown that memory defects in a fly model of intellectual disability can be reversed in adulthood (in an article published in the January issue of *PLoS Biology*). The researchers further demonstrated that the EHMT gene is a master regulator of learning and memory, which controls most of all currently known memory genes in fruit flies. While the implications for intellectual disability in humans need further investigation, these results are clearly encouraging for those aiming to develop therapies. Current research in Annette Schenck's group is expanding existing fly studies to include over 300 genes associated with cognitive disorders.

Two prestigious ERC Advanced Grants

Guillén Fernández of the Donders Institute has received an ERC Advanced Grant, together with Richard Morris of Edinburgh University. The grant will fund further investigation of the neural basis of knowledge acquisition and stabilization.

Max Planck Institute director Stephen Levinson, who is also an MPI Research Fellow at the Donders Institute, received an ERC Advanced Grant worth €2.5 million to study human communicative interaction.

More grants

Ivan Toni and Floris de Lange both won NWO Open Competition grants, each providing €200,000 of funding for a four-year PhD project. Hanneke den Ouden received an AXA Research Fund grant, which will allow her to continue her work as a postdoctoral researcher at the Donders Institute.

Two young international researchers, Murielle Ferraye and Guillaume Sescousse, received a Rubicon grant in order to work at the Institute. Another young researcher, Sara Bögels, who is currently working at the Donders Institute, also received a Rubicon grant, enabling her to spend a year at Glasgow University.

More at www.ru.nl/donders

Donders Backbone

Innovative technician – Erik van den Boogert

Due to its academic nature and high ambitions, staffing at the Nijmegen-based Donders Institute is extremely dynamic. Postdoctoral researchers and PhD students fly in from around the globe. Technicians, lab workers and research assistants form the much needed constant, the backbone of the institute.

If you're one of the many foreigners working at the Donders Institute you might be aware of a peculiar anomaly: when temperatures drop below zero and ponds, lakes and canals freeze over, the Dutch become really warm-blooded. Skating generates a degree of enthusiasm that is seldom seen in the Netherlands, apart from when watching the national football team. But whereas 'we' frequently lose important football finals, in speed skating the gold medals are often 'ours' for the taking.

If you've ever watched speed-skating matches on TV, you might have seen the meticulous recordings of each performance that are transmitted so quickly to the live TV programme. That requires a lot of technique...

This is, in fact, Erik's work. Erik? Yes, you know him. And if you don't, you should. Erik van den Boogert is head of the Technical Department at the Donders Centre for Cognitive Neuroimaging. He's the guy who was given the opportunity to build up the centre's laboratory facilities from scratch. He's proud of his team and committed to helping you to fine-tune the machines and computer systems to the needs of your experiments.

Erik van den Boogert

'I'm not a person to sit still. I really like to take advantage of each opportunity that arises – all week long. But I also like to focus my attention on different things.' Whether it's electric and magnetic fields at the Institute or accurate transponders at international speed-skating tournaments, Erik likes to apply innovative technical solutions.

Mountain biking is his most recent passion – and that of his family. In his office he has pictures of himself and his children taking part in cycling races in Germany and Belgium. Cycling is a very important part of his daily routines too: 'Rain or snow, I love the ride through the woods from my home to the Institute and back again. That's when I switch over between my one life and the other...'

Diary

7 April 2011, 16:00
Donders Lecture Svante Pääbo (Max Planck Institute for Evolutionary Anthropology, Leipzig)
Linnaeusgebouw, Heyendaalseweg 137, Nijmegen

6-8 April 2011
Toolkit of Cognitive Neuroscience: advanced course in functional neuroimaging data analysis
Centre for Cognitive Neuroimaging, Kapittelweg 29, Nijmegen

18-21 April 2011
Toolkit of Cognitive Neuroscience: advanced data analysis and source modelling of EEG and MEG data
Centre for Cognitive Neuroimaging, Kapittelweg 29, Nijmegen

26-28 April 2011
Toolkit of Cognitive Neuroscience: advanced topics in MR imaging of the brain
Centre for Cognitive Neuroimaging, Kapittelweg 29, Nijmegen

9 June 2011, 16:00
Donders Lecture by Sarah Blakemore (UCL, Institute of Cognitive Neuroscience)
Linnaeusgebouw, Heyendaalseweg 137, Nijmegen

22-26 August 2011
Toolkit of Cognitive Neuroscience: essentials of major neuroimaging techniques (EEG, MEG, fMRI, PET, TMS)
Centre for Cognitive Neuroimaging, Kapittelweg 29, Nijmegen

PhD defences

13 January 2011 - **Timmer, N.M.** The interaction of heparan sulfate proteoglycans with the amyloid ß protein.
14 January 2011 - **Crajé, C.** (A)typical motor planning and motor imagery.
10 February 2011 - **Scheeringa, R.** On the relation between oscillatory EEG activity and the BOLD signal.
4 March 2011 - **van Grootel, T.J.** On the role of eye and head position in spatial localisation behaviour.
4 March 2011 - **Bögels, S.** The role of prosody in language comprehension: when prosodic breaks and pitch accents come into play.
11 March 2011 - **Lamers, M.J.M.** Levels of selective attention in action planning.
30 March 2011 - **Van der Werf, J.** Cortical oscillatory activity in human visuomotor integration.
4 April 2011 - **Kuribara, M.** Environment-induced activation and growth of pituitary melanotrope cells of Xenopus laevis.
14 April 2011 - **Van Ossewaarde, L.** The mood cycle: hormonal influences on the female brain.
24 May 2011 - **Helmich, R.C.G.** Cerebral reorganization in Parkinson's disease.

Donders Institute Newsletter

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