Of mind and matter…

Oratie prof.dr. Sarah Durston

Universitair Medisch Centrum
Utrecht

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Entry music: Summertime by Gershwin

Played by Jaap Jan Steensma

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Mijnheer de Rector Magnificus, geachte collega's, dear friends and family, waarde toehoorders,

On this first day of summer, it is my privilege to address you all. As there are numerous friends and family members here who speak no Dutch, I will be holding this address in English. I trust that this will not cause the native Dutch speakers any problems.

"*I like nonsense! It wakes up the brain cells. Fantasy is a necessary ingredient in living, it is a way of looking at life through the wrong end of a telescope.*" This is a quote from Dr. Seuss. For a long time, he was my oldest son, Samuel's, favourite author and I used to read 'The Cat in the Hat' to him at dinner, to distract him from the fact he was eating vegetables. For those of you who do not know Dr. Seuss' work, he wrote many children's books, often in rhyme, always amusing and with simple statements that are often surprisingly relevant to a great many topics, including several that I want to discuss here today. This quote to me is all about science and what science should be about: It should be about picking up life and trying to look at it through the wrong end of a telescope. It should be about using our imagination to try to work out what it is we are looking at. And above all, using our imagination to that end should be fun! So that, Ladies and Gentlemen, represents the first goal of my address: I would like you to leave this auditorium in 45 minutes time thinking that science is fun!

Of children and their families

I also have a second and more serious goal in mind for this address: Imagine –if you will - a child with a developmental disorder, a child with Attention Deficit Hyperactivity Disorder or ADHD, for example. He – because ADHD is more prevalent in boys - has symptoms that make his life difficult. He may not be very good at paying attention; he may have trouble sitting still in class; he might not let others complete their sentences before blurting out his own thoughts. It is not that he does not want to sit still; or that he does not want to listen to what others are saying. He simply can't. His teachers may well get angry with him. His classmates will find him difficult to get along with; he may have trouble making friends. The point I am making is that children with developmental disorders have a hard time. In this day and age, there is an increase in the number of stimulants and other psychotropic medications being prescribed to children. This has led to suggestions that we as a society are 'over-medicalising' our young people. It has led to the public - and politicians in their wake - calling into question whether disorders such as ADHD even exist. It even led to political decisions where financial support to help these children– 'het rugzakje' in Dutch – was cancelled.

Of course, the dramatic increase in the prescriptions of psychotropic drugs to children is worrying. It seems unlikely that this reflects a true increase in the incidence of these disorders and it therefore suggests that over-diagnosis is taking place. That is why it is so important that children suspected of having a developmental disorder are seen by a

clinician who is properly trained to diagnose these disorders. However, the possibility of over-diagnosis does not preclude simultaneous under-diagnosis. There are still children who need help and are not getting it, because their problem is not sufficiently recognized. For them, a society questioning the validity of developmental disorders makes life even more difficult, because their parents may well be less likely to seek help. This societal attitude also makes life difficult for the children who are getting help and who need their medicines to be able to function. It makes life difficult for their parents, to whom we are suggesting that it is their parenting skills that are to blame. It is these children I would like you to keep in mind for the remainder of this address, because it is them we should think about most when we study the biology of developmental disorders. Therefore, my second goal for this address is to convince you that research on developmental disorders matters, and that it matters because we can use it to help affected children and their families.

Of categories and neurobiology

As a field, we have been studying neurodevelopmental disorders for at least 30 years, and we have learned a lot. We know that ADHD is associated with smaller brain volumes, on average. We know that there are changes in certain neurotransmitter systems in ADHD, on average. We know that children with autism have larger brains, on average, and that they are more likely to pick up details in a visual scene than the big picture. However, what we do still not know is how an imbalance in neurotransmitter systems comes about in an individual child, or how such an imbalance then leads to symptoms of ADHD. Not only is there the hotly debated gap between mind and matter, between symptoms and neurobiology; we do not even truly understand how the neurobiological changes come about. Why is that? One reason is that not all children with ADHD or autism are equal. Clinically, symptoms vary widely. You can compare two children with identical diagnoses and they will more than likely have different symptoms, different co-morbidities and respond differently to treatment. This is because neurobiology does not adhere to diagnostic categories. The current version of the diagnostic handbook in psychiatry, the DSM-IV, was designed to help clinicians have a way of standardizing diagnoses across countries, across clinics, and across individuals. It was not intended to map onto neurobiology and it is therefore more than likely that it doesn't! Yet, this is how we have traditionally gone about our research, by comparing groups of children with a DSM-diagnosis to groups of children without one. It is not surprising therefore that we have not always found satisfying answers, with clear-cut and replicable differences between groups.

One way out of this conundrum is to pick up Dr. Seuss' proverbial telescope and to look through the wrong end of it: If we recognize that there are probably multiple biological subtypes within diagnostic categories, that different neurobiological pathways may lead to similar symptoms then we can investigate this.

To give an example, Patrick de Zeeuw from our lab did a study where he addressed whether we could find subtypes among children with ADHD with different neuropsychological profiles. This study was based on a model of ADHD suggesting that there are at least three brain networks whose disruption might lead to symptoms of the disorder. Anatomically, these networks have more connections within them than between them and they have been linked to discrete cognitive functions: The first network is linked to cognitive control, our ability to control our behaviour. The second network is related to the way our brains process reward. The third network is linked to timing. We hypothesized that if deficits in these networks could lead to symptoms of ADHD independently of each other, then children with ADHD should have deficits in one but not all of these functions. Nearly everybody in our lab worked together to test 150 children on a neuropsychological battery testing these functions; cognitive control, reward processing and timing. Patrick found that there were independent factors contributing to the variance in the data, and that three of those factors mapped onto the cognitive functions we had predicted.[1] When he tested how many of the children with ADHD in the study had a deficit on one or more of these factors, there were no more children with a deficit on more than one factor than would be expected by chance – only six children in all. So, the findings from this study support the idea that ADHD

might be related to different brain systems. They support the idea that ADHD might be so heterogeneous, because the brain systems involved are not the same for everybody. As Dr. Seuss said: "*Why fit in when you were born to stand out?*" Not all children with ADHD are equal. The brain systems involved may differ between them. If you can find out which brain system is involved in an individual child, then you can use this knowledge to try to target that specific system. For example, if you have a child with ADHD who is sensitive to reward, but only when it is administered with high frequency, you might be able to use that in his treatment. You could use a behavioural program where he can earn frequent rewards with good behaviour. This is a useful parenting strategy with young children – it works wonders with my four-year old and my two-year old is also beginning to catch on - and similar programs have been used with varying success for treating children with ADHD. These findings suggest that it might depend on which brain system is involved in the individual child with ADHD whether a treatment strategy is useful.

As a second example of how you might narrow a diagnostic phenotype to get at the underlying neurobiology, I would like to touch upon the work of Marieke Langen and Tamar van Raalten in our lab on autism. They have taken a somewhat different approach to this problem: They have narrowed down the phenotype by focusing on a particular cluster of symptoms. As you may know, autism is characterised by three clusters of symptoms: Impairments in social behaviour, language impairments and repetitive and stereotyped behaviour. The research that Tamar and Marieke are doing focuses on repetitive and stereotyped behaviour. To give you an example of what I am talking about: we all

have our rituals and habits. It's human nature. I like to start my day with a cup of tea and get fairly disgruntled if I can't have it. For children with autism this can take on extreme forms, to the extreme where they always have to have their toys lined up in the same order at bedtime for example, or where they will not go to school if the furniture in the classroom has been rearranged. This behaviour is linked to frontostriatal systems in the brain. So in their research Tamar and Marieke focus on investigating the role of this circuitry specifically in these symptoms, using structural and functional imaging. I will speak more about this work later on.

In sum, psychiatric phenotypes do not map onto neurobiology directly. Different brain systems are involved in different aspects of psychiatric phenotypes, and to which extent these systems are involved is likely to vary between individuals, even if they have the same diagnosis.
A second point I would like to make is that most psychiatric symptoms can be conceptualised as extreme forms of normal behaviour, like the rigid behaviours I was just talking about. Dr. Seuss said: "*We are all a little weird and life's a little weird.*" In researching developmental disorders we can use that fact to investigate the extent to which symptoms are on a continuum with typical behaviour. More on that later as well.

Of cause and consequence

One thing that we as a field have been particularly interested in is investigating how risk factors for developmental disorders affect neurobiology. One way investigators go about this is to select genes that have been associated with a disorder and to investigate how their impact on brain anatomy or brain function. However, it is important to realise that the odds ratios for these genes are very small. That means the increase in risk of developing ADHD if you have the risk allele is only tiny. For example, for one gene that has been associated with ADHD, the DRD4 gene, the chances of developing ADHD if you have the risk allele go from 4% in the general population to 4.5% for carriers of the allele.[2] Interestingly, there is some evidence to suggest that certain risk alleles might also relate to different subtypes of ADHD. For example, for the DRD4 gene, it has been shown that among children with ADHD, carriers of the risk allele are those with better neuropsychological functioning.[3] We have done a number of studies where we have linked risk genes to neuroimaging measures. Given, the small risk these genes convey, you might think this is likely to be a fairly hopeless undertaking. As it turns out, it's not. When 'imaging genetics' - as this type of study is called - was developed, the pioneers argued that it should be easier to pick up gene effects in neuroimaging measures, as these are more closely related to gene expression than a diagnostic category is. They argued that because of this, you should be able to do studies with fewer subjects than typical genetic studies –with between 40 and 100 subjects rather than thousands - and still pick up gene effects. Indeed, it has been our experience that you can pick up the effects you are interested in with limited numbers of subjects.

For example, in one older study that I did with a number of my collaborators here today, we looked at the effects of the same DRD4 gene on brain volume in 78 subjects. We also looked at the effects of a second gene, the DAT1 gene. Why did we pick these two candidates? They can't have been the only two genes that had been linked to ADHD at the time? Indeed they were not. However, they were both strong candidates for ADHD risk genes as both had been shown in meta-analytic studies combining data from thousands of subjects to be associated with increased risk. But just as importantly, these two genes had regionally specific expression patterns in the brain: they were expressed more in some brain areas than others. That gave us a very clear hypothesis of where in the brain we would expect their effects. And indeed, the results confirmed what we expected: these genes did have an effect on the volume of those brain structures where they were expressed. Furthermore, they did not impact the volume of other structures.[4] This type of study can set you on the path of mapping the causal cascade, from a change in genetic architecture to subtle neurobiological changes and from there – hopefully – towards cognitive and behavioural changes associated with the phenotype.

Another way to get at causal pathways in developmental disorders is to use naturalistic experiments. One example is studies of children who were internationally adopted after living in an orphanages rather than family homes in countries of origin. Many of these children were adopted to Western European countries and to the US, but even when they are raised in loving, caring homes, these children have many more behavioural problems and diagnoses of developmental disorders than their peers. Here it is not genes that are to blame, but rather early life

experiences. My friend and collaborator Kathleen Thomas from the University of Minnesota has been interested in comparing children with early deprivation to their peers. She and her group recently compared children adopted from Rumanian orphanages relatively early in life to those who were adopted relatively late and showed that specifically memory systems in the brain were affected by longer deprivation.[5]

So in sum, neuroimaging can be used to investigate the impact of risk factors for developmental disorders on the brain, bringing perhaps a neurobiological edge to Dr. Seuss' comment "*I'm sorry to say so, but, sadly it's true, that bang-ups and hang-ups can happen to you.*" It is important to realize that it is not just our genes that shape our brains. It is also what happens to us as we are growing up. So with that I will move on to the next part of this address:

Of development and why it matters

Why does development matter in studying developmental disorders? Why beleaguer children with these disorders – who are having such a hard time anyway – by asking them and their families to spend time participating in scientific studies? Why not simply study adults with the same disorders to see what is wrong with their brains? The reason is that the answer to the question 'what is wrong with the brain in autism?' or 'what is wrong with the brain in ADHD?' may well depend on the age at which you ask it. To take the example of autism: On average, the brain is slightly bigger in children (or adults) with autism than in persons without this disorder. However, there is evidence from a number of groups now that very early in life, the brain is not larger in individuals who go on to develop autism. It may even be smaller. It does not begin to look bigger until about the age of 2 years.

In our own lab, we have seen a similar pattern later in life in autism: In work that Marieke Langen did for her thesis, we found that differences in the striatum in autism become more pronounced in the course of adolescence. In this period of development, the volume of striatum typically decreases. However in individuals with autism, the volumes stayed stable, or even increased.[6] Now these were cross-sectional data, but Marieke has just completed a longitudinal study where she shows the same effect *within* individuals. And here, interestingly, repetitive and stereotyped behaviour at the time of inclusion in the study actually predicted the *change* in striatal structures: the volume of caudate nucleus increased most for those

individuals who had the most repetitive symptoms, suggesting perhaps that it is the behaviour that is driving the pattern of brain development and not only the other way round. So it pays to look at development, and to look at it within individuals. Dr. Seuss said it: *"Adults are obsolete children"* and by this he was making the point – not only that some grown-ups could benefit from looking to their inner child – but that people are the result of their own developmental process.

We can learn a lot about the outcome of children with neurodevelopmental disorders from studying their brain developmental trajectories. A nice example of this comes from the work of my friends and colleagues Drs. Giedd, Gogtay and Shaw: At the National Institute for Mental Health in the US, they have collected longitudinal data from literally hundreds of children, both typically developing and with developmental disorders, and they have used these data – among many other things – to show that there are differences in the developmental trajectories between children with ADHD who no longer meet criteria for the disorder in adolescence, and those who do. Here, part of the parietal cortex, an area of the brain that is particularly relevant for attention, has a more typical developmental trajectory for those individuals who no longer meet the criteria for ADHD as adolescents, suggesting perhaps that their brains are 'normalising'.[7] So, development matters. *"A person's a person, no matter how small"* said Dr. Seuss and what happens to that person as he grows up shapes him and his brain.

In a recent reorganisation, the Department of Child and Adolescent Psychiatry and the Department of Psychiatry at the University Medical Centre Utrecht merged to form a larger Department.

The key motivation for this merger was that we can now offer continuous care to patients over the life span. Patients no longer need to switch to a new department with a new doctor and a new clinical team when they turn 18. In addition to making good sense for our patients, this reorganisation is particularly exciting to me in the research possibilities it offers: we will now be able to follow-up individuals with developmental disorders more easily, to track their brain development but also link this to the waxing and waning of their symptoms, and their cognitive profiles. It gives us the opportunity to truly study neurodevelopmental disorders across the life span.

Of nodes and networks

One key shift in the field of psychiatry in recent years has been to recognise that the brain is a network. The brain contains about one hundred billion neurons or nerve cells. That is a 1 with 11 zeros! But it contains many more synapses, as many as one hundred trillion for an adult. That is a 1 with 14 zeros. And ten times as many again for a child! That makes an average of 7000 connections for each nerve cell in the brain. From that fact alone, it is clear that the brain developed to communicate – for the neurons to talk to each other. Brain function is reflected in its networks. Traditionally, we have used neuroimaging to compare brain volume or brain activity between groups, asking questions like "is the frontal cortex smaller in children with ADHD? Or: is the amygdala less active in autism?" But over the last few years, the development of new MR techniques and analysis approaches has permitted us to address the true nature of the brain more by analysing its network properties. Some of my colleagues in Utrecht working with Professors Hulshoff Pol and Kahn have been at the forefront of developing advanced techniques to be applied in psychiatry. These include René Mandl, who has developed a technique to look at the activity of white matter tracts, Martijn van den Heuvel who uses graph theory to develop mathematical analysis methods and Hugo Schnack who has developed accurate anatomical quantification methods. My friend and colleague Professor Kerstin Konrad from Aachen University has used network analyses to look at brain networks in ADHD for some of the concepts I spoke of earlier: cognitive control and time perception.

Her group found that there was indeed a reduced coupling between activity in key regions of the networks underlying these abilities in ADHD. In our group, Dienke Bos is studying the development of networks in developmental disorders. In her PhD-project she is collecting longitudinal functional MRI scans from typically developing children and children with ADHD and autism to perhaps link network development to cognition and symptoms, rather than merely the development of brain structures.

So it matters to realise we are studying networks. We are not simply studying an organ composed of different structures and cell types, but rather it is the communication between those cells that is critical to its function.

Of challenges and opportunities

The types of analyses I am talking about involve huge datasets and computationally demanding analyses. Studies including hundreds of subjects are not unusual and we are moving towards even greater computational demands, as key fields such as genetics and neuroimaging are now being combined. Although this seems like a challenge in itself, the pace of technological development is phenomenal and it is not really a question of whether this is technically feasible – it is. However, this does present other challenges to our field, as answers do not come falling out of large datasets merely by their size. The answer one gets depends entirely on the question one asks. One illustration of this can be found in the autism literature: Autism is the most heritable of all developmental disorders, with an estimated heritability of 90%! For most psychiatric disorders heritability is estimated well below that – at 70% for ADHD for example[2] and 65% for depression.[8] When the mapping of the human genome was completed in 2003,[9,10] there was great faith in the field that we would soon know the genes for many psychiatric disorders, and especially for ones as heritable as autism. However, finding the genes has proven to be extremely difficult. This phenomenon is referred to as 'the problem of the missing heritability': How can disorders be heritable, run in families, in the case of autism with heritable factors explaining up to 90% of the variance, and it still prove so hard to locate the genes involved? Maybe we need to look through Dr. Seuss' telescope backwards: Three papers published back to back in Nature recently set a step in that direction:[11,12,13] they showed that for some children with autism – so not for everybody with the

diagnosis, probably for about a quarter of affected individuals – there was an important role for genetic mutations that were often passed down from the father. And importantly they showed that it mattered in which genes these mutations occurred; they were most common in genes that were functionally linked: all were involved in early development. What these papers did was to combine clever hypotheses with a clever application of models. The authors put their imagination to work and by doing so they have pointed the field towards another way of thinking about heritability in autism. As Dr. Seuss put it: "*Sometimes the questions need to be complicated so that the answers can be simple.*"

To be clear: I am not saying that data-driven approaches are not useful. All I am saying is they do not do away with the need for a hypothesis. I will illustrate what I mean: Janna van Belle in our lab is working on how communication between brain areas changes over development. Investigators often approach this by looking at brain connectivity during rest; subjects lie quietly in the scanner while the data are collected. The question Janna has been asking is whether it matters what the person is doing in the scanner. Does the development of connectivity look the same when subjects are striving to do a challenging cognitive task as when they are resting quietly? To address this question, Janna has used a data-driven technique to identify brain networks. This technique identifies many networks per subject. But then we need to select which of these networks to study. How do we know which ones are related to the task, or to rest? Some of them relate to subject motion, or to scanner artefact, or to respiration. How do we know which ones? We need criteria to determine which networks to select, and a hypothesis can help provide them. In Janna's case, we were specifically interested

in networks involved in cognitive control, and so could select those networks that were related to task performance. In doing so, we could answer the question we set out to address: If you want to know how brain connectivity develops, does it matter what a subject is doing in the scanner while you collect the data? And the answer is, yes, it does. Developmental changes in connectivity look different when subjects are doing a task. And importantly, having a hypothesis helped us make the best use of this data-driven method.

Finally, I would like to touch on the opportunities offered by animal models. These are sometimes criticized in psychiatry, as it is argued that animals cannot display the same complex behavioural phenotypes as humans with psychiatric disorders, and even if they could, you cannot be sure the neurobiological pathway is the same. One clever way of looking at it through the wrong end of the telescope is to make animal models based on human genotypes. My collaborator and friend, Professor BJ Casey and her team at the Sackler Institute for Developmental Psychobiology, made an animal knock-in model of a human variant in a gene related to fear extinction. They showed that the animal model had the same phenotype as the human and linked it to physiological and neurobiological measures using neuroimaging and skin conductance in humans and freezing behaviour in mice.[14] Clever approaches like these can bring us closer to tying basic neurobiological mechanisms to complex human behavioural phenotypes. This is another opportunity in Utrecht, where we have basic cell and animal researchers integrated with clinically oriented researchers in the Rudolf Magnus Institute.

So to sum up: "*Think left and think right and think low and think high. Oh, the thinks you can think up if only you try!*" Dr Seuss said it right: hypotheses matter. Clever models matter. Thinking ahead of time about what you expect in a study matters, because that is the only way you can formulate the right questions and decide which measures you will need to collect.

Of plans and ambitions

Where do I hope we will go with the themes I have just talked about? And how do I plan to integrate them in my own research? Firstly, I think we need a more dimensional approach, where we address clusters of behaviours right through the typical range into their extremes. One way we are doing that in the lab is to not only look within disorders for relevant characteristics of the phenotype; we are also looking at symptom clusters across disorders. This is the PhD-project of one of our newer group members, Branko van Hulst. Secondly, development matters. The time has passed for us to merely compare groups of subjects with one another. As I have already alluded to, we are tracking children over time and looking at typical development as much as atypical development. This is the project of another new PhD-student in the lab, Lara Wierenga. A third avenue of research that I think will prove useful is to track individuals as they develop neurodevelopmental disorders. This is challenging by definition, because how do you identify those individuals who will develop a disorder among their peers? In our lab, Sanne de Wit is now conducting the third follow-up of young adolescents who were at risk of developing psychosis based on their clinical profiles. Her subjects are now in their early twenties. She is analysing longitudinal brain measures from them and I am happy to be able to report from her preliminary data that a third of the at-risk subjects are complete remitters, meaning they have no symptoms whatsoever left at follow-up. Even among those individuals who had a psychotic episode, 30% had no more symptoms at follow-up. Potentially good news for those adolescents who go through such an episode, and for their parents.

One exciting development in Utrecht that will offer opportunities for tracking individuals as they develop disorders, are the plans for the 'Youth Centre'. Here, thousands of young people will be followed with a focus on their brain and psychological development, some of them from before birth. This will not only teach us a great deal about typical brain development, but will also provide a unique opportunity to study how some of them develop the disorders I have talked about, what factors contribute to these disorders, as well as which factors might be protective.

Of children and their families once more

As I near the end of this address, let us return to the children with neurodevelopmental disorders with whom I began: How is the work I have talked about today benefitting them? Well, at the moment, indirectly, if I am honest. I am a neurobiological scientist and I do honestly believe that by understanding the neurobiology of developmental disorders better, we will be able to develop new treatments, that we will be able to define biological subtypes, and that we will be able to predict based on neurobiology which treatment will work best for whom. That is a very important reason for doing the work we do. However, this is going to take time. It has taken 30 years to get to where we are now and new treatments and personalised medicine will not be here tomorrow. However, there is a second way that this research is important for children with developmental disorders and their families: it is showing us that ADHD and autism, and other developmental disorders have a biological side. These disorders are not merely the result of a society focused on keeping children meekly in a classroom, or of parents unwilling to invest time in their children. Of course, there are still people who say that as long as we have not bridged the gap in our understanding between symptoms and neurobiology – between mind and matter-, we cannot claim that these disorders are neurobiological. However, the type of research I have talked about today is providing support for the idea that biology does tie into symptoms. By looking through the wrong end of a telescope and formulating clever hypotheses,

we can then test them and close in on that gap. This matters because understanding that there is a biological mechanism can be of support to affected children and their families. It matters that the classmates of these children understand that the boy who will never let them finish a sentence is not cutting in to be annoying, but because his brain works a little differently. Having a biological cause is not the same as saying there is no possibility for improvement, or that the only possible treatment is to prescribe medicines. Realising that matters too. For these kids I would like to quote Dr. Seuss again: *Be who you are and say what you feel, because those who mind don't matter and those who matter don't mind.* Children are individuals and need to be respected as such, just as much as adults. Sometimes some children need a helping hand on their individual developmental trajectories. And this type of research will help us to help them better.

Now, for the final part of this address:

Of those who matter most to me
(or Word of thanks),

where I will address everyone in the language in which I usually communicate with them.

De Raad van Bestuur van het UMC Utrecht en het College van Bestuur van de Universiteit Utrecht wil ik bedanken dat ze deze leerstoel in het leven hebben geroepen, en dat u mij daarop benoemd heeft. Ik ga mijn best doen er een goede invulling aan te geven.

Geachte Professor van Engeland, beste Herman, Hartelijk dank voor je uitgesproken vertrouwen, en voor het gegeven dat je vertrouwen altijd voelbaar was, ook op de momenten dat je deze niet uitsprak. Ik heb me daardoor zeer gesteund gevoeld.

Geachte Professor Kahn, beste René, Ik heb bewondering voor de manier waarop je de dingen doet. Ook in de recente reorganisatie heb je mij –en ik vermoed met mij velen- verrast met je verfrissende insteek. Ik vind het een uitermate positieve ontwikkeling dat je je weer meer met wetenschap gaat bezighouden en verheug me erop om met je samen te blijven werken.

Geachte Professor van Ree, beste Jan, jij zei mij eens dat ik niet zo ongeduldig moest zijn. Tja, dat is nou eenmaal de aard van het beestje. Hoewel je vond dat ik teveel haast had, heb je me gesteund en gepromoot op de juiste momenten. Dankjewel.

Geachte Professor Joëls, beste Marian, met jouw komst is er een rolmodel bij in Utrecht - voor jonge, vrouwelijke onderzoekers, maar ook zeker voor de mannelijke! Ik ben heel blij met je betrokkenheid, je oprechtheid en je doortastendheid. Dankjewel.

Geachte Professor Hulshoff Pol, beste Hilleke, bij jou ben ik mijn wetenschappelijke loopbaan begonnen. Je was toen zelf net gepromoveerd en begon aan je eigen carrière. Ik vind het bijzonder dat je van stage-begeleider mijn co-promotor bent geworden, toen collega, en dat ik nu tegenover je op de hoogleraarsgang zit. Dankjewel voor je collegialiteit. Ik verheug me erop nog vele jaren met je samen te werken.

Geachte Collega's van de nieuwe afdeling Psychiatrie, of om in UMC termen te blijven: Psychiatrie 3.0. Verandering staat niet altijd gelijk aan verbetering, maar soms ook wel. Of onze nieuwe afdeling ook een betere afdeling wordt bepalen wij zelf. Met een heel aantal van jullie werk ik al jaren met veel plezier samen, ik heb er vertrouwen in dat dat met deze reorganisatie alleen maar meer zal worden.

Dear Professor Casey, dear BJ, You have been a true mentor and a true friend. Thank you for welcoming me into your lab and your life more than a decade ago. My life, as well as my science, has been the richer for it.

My dear friends from abroad, Jay, Nitin, Philip, Kerstin, Katie and BJ, who kindly agreed to be here today and to speak in a symposium, so that you could listen to me for 45 minutes: Thank you for coming! It means much to me that you did.

My lab, you routinely remind me that while science might be fun I do not seem to have much time for it anymore! Thankfully, none of you seem to have been too intimidated by my new title and you still knock on my door if you have something too good to wait! The science that gets done in the lab gets done by you! And by that I do not mean only the faculty, post-docs and PhD-students, whom I have already mentioned today, but also the research assistants and the students who are at least as critical to the process as the others.. Science is, above all, a team effort!

Today, it is a little over 18 years ago that I sat in this auditorium and listened to the first Oratie I ever attended. The speaker was the first Professor Durston to be appointed at Utrecht University and my father. At the time, I was not yet 20 and still convinced I did not want to do anything with my life that my parents had done with theirs (namely science, teaching, or working at a university or any other bureaucratic institution!). I guess I am a case in point for the influence of genes and positive parenting on development! Dear Mum and Dad, it is a testimony to your patience with me – and all of us – that you have never reminded me of this fact over the past two decades. Thank you for your love and support.

My dear Sisters, Rebecca and Emily, and my other relatives here today, dear friends, I can always tell you are proud of me and that means a lot. You show it again in being here today, even if it meant international travel. Thank you.

Lieve Bart, Je zit in een parallel traject aan dat van mij; een gegeven dat ons leven – en zeker de logistiek daarvan - wel eens ingewikkeld maakt. Maar uiteindelijk komt alles steeds weer samen: ik vind het dan ook een mooie cirkel dat mijn nieuwe bureau op mijn nieuwe hoogleraarskamer op precies dezelfde plek staat voor hetzelfde raam waar jij meer dan 15 jaar geleden als jonge promovendus begon, op de kantoortuin waar wij elkaar ook hebben ontmoet. Dankjewel voor je steun en liefde. Zonder jou had ik hier vandaag niet gestaan.

And of course, my boys, dear Samuel and dear Ewan; they are the best reminder of what really matters, and why I don't mind so much about the rest of it. They thought this party was so boring that they have gone to play in the garden. It's a perfect incentive for me to stop talking now so we can all go to join them!

Ladies and Gentlemen, as Dr. Seuss said: *Fun is good!* I hope you leave this beautiful auditorium with - first of all - a sense that science matters, and that studying neurodevelopmental disorders matters. But also with a sense that science can be fun – and not only because of the fancy dress!

Now, I would like to invite you to the reception in the beautiful cloister gardens, where I hope the first day of summer will smile down on us.

To end with one final quote: "*I have meant what I said and I have said what I meant.*" Thank you all for your attention. Dames en Heren,

Ik heb gezegd.

Of my sources and inspiration
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15. Seuss Dr. Whole oeuvre.

Colofon

Uitgave

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Opmaak

Multimedia, Facilitair Bedrijf, UMC Utrecht

Druk

ZuidamUithof Drukkerijen, Houten

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UMC Utrecht

Bezoekadres:
Heidelberglaan 100
3584 CX Utrecht

Postadres:
Postbus 85500
3508 GA Utrecht

www.umcutrecht.nl

Prof.dr. Sarah Durston (1974) was appointed as professor of Developmental Disorders of the Brain on April 1st 2011. She graduated from Utrecht University specialising in biological psychology in 1996 and continued at the the University Medical Centre Utrecht to do her PhD on ADHD, under the supervision of Professors van Engeland, Buitelaar and Hulshoff Pol. During her PhD she worked as a fellow with Professor Casey at the Sackler Institute for Developmental Psychobiology in New York. Upon completing her Ph.D. in 2003 she became a faculty member at the UMC Utrecht and started her lab, NICHE. She still works there today and continues to be an affiliated faculty member of the Sackler Institute.

Prof.dr. Sarah Durston (1974) werd op 1 april 2011 benoemd als hoogleraar Ontwikkelingsstoornissen van de Hersenen. Zij studeerde in 1996 af aan de Universiteit Utrecht in de biopsychologie and promoveerde vervolgens op ADHD bij het Universitair Medisch Centrum Utrecht, onder begeleiding van de hoogleraren van Engeland, Buitelaar en Hulshoff Pol. Tijdens haar promotie werkte zij als fellow bij Professor Casey op het Sackler Institute for Developmental Psychobiology in New York. Na haar promotie in 2003 werd zij staflid bij het UMC Utrecht en richtte zij haar lab NICHE op. Naast haar aanstelling op het UMC Utrecht en is zij nog altijd verbonden aan het Sackler Institute.