Back to the roots: childhood as the source of both vulnerability and resilience

Dies lecture given by

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during the 443rd Dies Natalis

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Universiteit
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Esteemed Rector Magnificus, thank you for your introduction.
Distinguished audience,

Stress?
Today we are celebrating the 443rd anniversary of the foundation of Leiden University, our Alma Mater. It was 443 years ago, in 1575, that the University was inaugurated, at 7 o'clock on a cold morning in this Leiden Pieterskerk in the midst of the Eighty Years' War with the Spanish: altogether a very stressful period. In 2018 we are fortunate enough in the Netherlands not to have suffered war for some time. We have enough to eat, we live in a democracy and almost everybody has access to medical care. But, in spite of all these achievements, there is one enemy we have not yet managed to defeat, and this enemy is '*stress*'.

Is there anyone here today who hasn't felt stressed over the past year? It can hardly have escaped your notice that even in the 'ivory towers' of academia, life is becoming increasingly frenetic and hectic. From professors to students, we all seem to be experiencing higher levels of stress. Let me give you a few figures: in 2013, 49% of all students indicated that they suffered from psychological complaints, with depressive symptoms topping the list.[1] By 2017, the majority of students surveyed (74.8%) said they experienced 'high to very high' levels of emotional exhaustion.[2] And the situation of our PhD candidates isn't much better: according to the Leiden Centre for Science and Technology Studies, 38% of them have an increased risk of mental problems.[3] With 6,700 members of staff, including PhD candidates, and 28,130 students in Leiden, that adds up to a lot of hours of stress, worry, sadness and sleepless nights. I hardly need to say that all this leads to sick leave and study delays, which in turn cause more grey hairs for those responsible for running the University!

Although this is not exactly a cheerful topic for a birthday party, such as we are celebrating here today, it is important to recognise what is going on, and especially to give some thought to what we can do about it.

As a professor of Stress-related Psychopathology, I have been studying the topic of 'stress' for many years, and it's something that gives me great satisfaction. My research focuses on factors that contribute to the development of stress and psychological problems and their consequences. This field is by its very nature interdisciplinary, because the influence of stress extends to many different domains, both physical and mental. I've been fortunate enough to work in my discipline of Clinical Psychology with colleagues from a range of different disciplines, from neuroscience, epidemiology, psychiatry and radiology to education and child studies. I've also been part of a range of different consortia, including the Netherlands Study of Depression and Anxiety (NESDA) and the Mood and Resilience in Offspring project (MARIO), and in such collaborations as the Leiden Institute for Brain and Cognition (LIBC). I would like to take this opportunity to share a few of our findings with you, in the hope that some of these insights will be relevant for our University, our Alma Mater.

What is stress?
The ability to handle stress is an essential requirement for life. But what exactly *is* stress? Stress is defined as every process that disturbs our 'homeostasis', our stability. Although stress has negative connotations, in its purest sense it is neither intrinsically good nor bad. Having our stability disturbed is a necessary condition for change, and a crisis at the right time can provide all kinds of useful insights and lead to important innovations, depending on how we handle it.

Stress is a rather confusing term, because it refers to three different factors:
1. The **input**: the cause, the stressor
2. The **process:** how we deal with the situation, including all the hormonal processes in our body and brain
3. The **output**: the emotional, cognitive, behavioural and physical consequences, including adaptation and recovery

The input: the stressor

In animals it is very clear what switches the stress system on: everything that directly or indirectly endangers their existence triggers a stress response. Around the time that the University was founded there were many concrete threats to existence, such as famine and disease. In 2018 it is a somewhat dubious achievement that today we generate most of our stressors ourselves, often via our own thoughts: 'Too often we suffer most sorely and thereby feel most poorly from dreaded aches and pains.' Our stress system can be activated by a broad and highly individual spectrum of stressors, shaped by our previous experiences. We have little influence on the content of this range of stressors. One person may suffer intense anxiety facing a room full of first-year students, while another is deeply affected by a critical comment, and yet another feels his stomach churn with distress when he sees his colleagues go off for lunch and he isn't invited to join them. In spite of the individual nature of many of our stressors, research has shown that there are two general traits that trigger almost every stress system: we are extremely intolerant of uncertainty[4;5] and we find it hard to cope with rejection, criticism and exclusion.[6-8]

The good news is that the reverse is also true; the opposites of uncertainty and rejection, both in terms of control and self-determination, as well as social recognition and support, are powerful tools to counteract stress. And you can take this very literally: the physical presence of a good friend or partner can reduce the physiological stress response by half.[9] This is something worth remembering if you see a colleague pacing about in the corridor with steam coming out of her ears. I will come back to this later.

The process

In the animal kingdom, where stressors can be life threatening, the ability to fight or flee immediately is essential for survival. The cascade of hormonal responses from the HPA axis (cortisol) and the adrenergic system (adrenaline) that are triggered and their impact on the brain have been described in detail, including by eminent Leiden researcher Professor Ron de Kloet and his research group.[10]

In our Clinical Psychology unit we conduct research on the *human* brain, where the processes are surprisingly similar to those in animals. When we experience acute stress, the stress hormones cortisol and adrenaline cause the brain to make a myriad of subtle neural changes. We are all more than familiar with the effects of these changes. Beside a sudden rise in blood pressure and a more rapid heartbeat, after a stressful event those areas of the brain that are important for emotional memory and regulating emotions are also activated. At the same time, complex cognitive functions are less active[11;12], and with good reason: when you are face to face with a hungry lion, the seriousness of your situation will not be helped by remembering the names of the last ten presidents of the United States! If an individual who has just performed a stressful task then looks at photographs of emotional events, such as a stabbing or a bleeding hand, while being monitored in a scanner, extra activation can be seen in the amygdalae.[13] These are the almond-shaped nuclei of the brain that are crucial for emotional memory. From an evolutionary perspective this is an ingenious mechanism: at times of stress it allows us to store information securely in our brain. This information can also be relevant for potential future dangers. However, the system does have some disadvantages: all those instances of stress - that we would most probably prefer to forget - are etched firmly in our memory, while the pleasant moments have to make do with a much weaker memory trace.

Our learning strategies also change during acute stress.[14] While under normal circumstances we mostly rely on the (hippocampus-dependent) cognitive memory system, when we are under stress we tend to switch over to less flexible (striatum-dependent), automatic, conditioned responses; we shift to automatic pilot. It is important to bear this in mind in certain professions, such as in aviation or law enforcement, where it is crucial that responses are both rapid and

appropriate, especially under stress. But in a university context, working on automatic pilot is not particularly beneficial for innovation or creativity.

Psychological consequences

What are the psychological consequences of stress? From a clinical perspective it is important to study the impact of particular stressors in everyday life, and to look at who is particularly sensitive to these stressors. This is not as simple as it sounds. It requires large groups of people to be carefully monitored and studied over a long period of time. The Netherlands Study on Depression and Anxiety (NESDA), in which over 3,000 people have been followed for more than ten years, is a unique study programme that has generated a wealth of interesting data. One of the intriguing findings is that the effects of stress (in this case depressive symptoms) can occur almost immediately following a stressful event (such as dismissal from a job or the death of a loved one), or in some cases the symptoms may not emerge until many years later. We found that of all the possible risk factors for depression investigated in the context of the NESDA study, the greatest stressors are not in the here and now, but in childhood.[8;15] Respondents who reported being raised by highly critical and/or emotionally neglectful parents were found to be far more likely to develop depression or anxiety 25 years later in adulthood. We also observed that the brains of adults who had been emotionally mistreated or neglected in childhood exhibited stronger stress responses when they were asked to look at threatening faces while being monitored in the scanner[16] or when they were excluded from an online ball game.[7] These adults also exhibited more avoidance, mistrust and anxiety in intimate relationships, especially when they had developed depressive symptoms. This is really quite tough, because this behaviour means that these individuals miss out on the support that comes from the most valuable weapons against stress: appreciation and social support.

Nature and nurture

Childhood, in particular the way we are brought up by our parents, seems to play a defining role in how we handle stress and our vulnerability to developing psychological problems later in life. In addition to an inherited genetic 'susceptibility', our level of sensitivity to stress seems to be 'programmed' in childhood. However, this is not a one-way street, because, while parents influence the working of their children's stress system via their parenting style, children, on the grounds of their own genetic profile and related character traits, will also provoke particular behaviour in their parents. We are currently examining these processes in the context of an interdisciplinary study among three generations of 63 families. The research falls within one of the research profile areas of the University and we are working on it together with colleagues from the Leyden Academy on Vitality and Ageing. We study the brain activity of parents and their children and try to determine to what extent the elevated sensitivity to stress in the brains of children who have been the object of frequent criticism by their parents can also be seen in the parents, and how this over-sensitivity plays a role in critical behaviour by parents towards their children.

The intergenerational perspective is an important but complex aspect if we want to gain a better understanding of depressive disorders. Recent research has shown that more than 50% of children whose parents have a history of depression will themselves develop depression before the age of 35.[17] These children not only have a genetic predisposition, but they also grow up in a vulnerable environment. In the national 'Mood and Resilience in Offspring' (MARIO) project, large-scale research will be carried out over the next eight years on the factors that play a role in the development of depression in these children, and we will be looking at how preventive E-health interventions can be used to counter this.

Young people and depression

How can these insights help a young person or a student suffering from anxiety or depression in real terms? How do we decide what the best treatment is for these young people? Who will benefit most from individual therapy, and when should parents be involved in the treatment? These are just some of the questions that we are currently working on with a team of PhD candidates and other researchers, in the context of a VICI grant. We use brain scans and innovative digital techniques to research parenthood in daily life. Using electronic diaries filled in by both parents and young people with depressive symptom, we chart how the mood of both of them influences their interactions, and conversely how these interactions affect the mood of the adolescents. The next step, which should happen quite soon, is to develop personalised parenting interventions based on the findings. One parent might, for example, receive a digital message prompting him to initiate some positive contact with his child, while another might be reminded that the child should get some exercise. This work is closely linked to the Digital Society Research Agenda, which aims to maximise the use of digital resources to make our society more resilient and sustainable.

Alma Mater

These are a few examples of the research we are currently working on. I would now like to turn my attention briefly to our Alma Mater on this, her birthday, and to look at whether we can do something about the stress that weighs so heavily on her and her academic 'offspring'. Let me start by returning to the number one arch enemy of our stress system: uncertainty. Our natural tendency is to eliminate causes of stress; indeed, it is something that policy-makers have made a career out of. In times of stress we try to counter the impact by tightening our control over our environment. We do this by making rules, taking safety measures, and drawing up all kinds of procedures, guidelines, instructions and laws. We see this tendency all around us, from border controls to childcare centres, from playgrounds and classrooms to operating theatres, and I fear that our Alma Mater is no exception to this rule.

Paradoxically enough, imposing even more rules and guidelines only leads to greater stress and gnaws away at our sense of trust and control.

Moreover, uncertainty may well disturb our sense of balance and cause stress, but learning to tolerate uncertainty and exploring without knowing exactly where you will end up is crucial for both teaching and research. In searching for solutions ourselves, we are forced to rely on other qualities, both in ourselves and others. And failure can itself lead to important insights and innovations.

There are some excellent opportunities available to our Alma Mater. Alma is the feminine form of the Latin word *almus*, which means 'bountiful', from *alere* ('to nurture), so the Alma Mater is literally the 'nurturing or caring mother'. Just as over-critical parents who lack warmth will raise children who are at greater risk of depression and anxiety, our Alma Mater can also play an important role in stimulating the wellbeing of her academic 'offspring'. Not only in nurturing them with knowledge, but also by teaching them to handle challenges and uncertainty, by offering them solace for the pain of failure and by expressing appreciation for success, at whatever level that may be.

I am well aware that I am but a young novice compared with our Alma Mater, with her respectable 443 years. Nonetheless, I would like to share some recommendations for a resilient university.

Highly esteemed Alma Mater,

- The University originally began as a bastion of freedom. Work on the basis of trust and confidence, and give responsibility and direction rather than imposing more control and rules.
- Uncertainty is *the* breeding ground for brilliant ideas and

innovation. Teach your 'academic children' to tolerate and recognise the value of uncertainty; let them experience what it is like to stray from the well-trodden path and even to fail.
- Stimulate ambitions, but at the same time reduce stress by promoting collaboration and exchanges.
- Express your appreciation, and encourage people at all levels, from students to deans, to give voice to their appreciation.
- Promote an ambitious study culture, but at the same time show care and concern for the psychological wellbeing of students and PhD candidates.
- Don't only celebrate the major successes, but once in a while organise a 'failure party' for courageous failures.

In conclusion, I wish our Alma Mater and all of you present here today a truly splendid year.

I have spoken.

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Stress can really throw the brain off balance. Research in the last few years has shown that the brain responds strongly to stress, especially to uncertainty and social rejection and exclusion. Conversely, the opposites of uncertainty and rejection – control and self-determination, and respect and social support – are powerful weapons to combat stress. Sometimes the effects of stress will pass quickly, depending on previous experiences and genetic (in)sensitivity. Often, however, chronic stress and trauma, especially in childhood, will in the long run lead to an over-stimulated brain, with all its associated consequences, including depression and anxiety problems. These effects can also have an impact on the next generation: important risk factors here are not only genetic defects but also growing up in a vulnerable environment.

Stress is an exciting theme for interdisciplinary academic research. At the same time, it is also a topic to which we can personally relate. This is not always a simple matter, given the high prevalence rates of stress and psychological problems among university staff, PhD candidates and students. In view of recent research findings on vulnerability and resilience, what possibilities would there be for creating a (more) resilient university?

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