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Prologue

There are many ways to describe my grandfather, but above all, he was a very special man.
He was a Director of a technical school and quite an authoritarian. His emotions were intense and he tried to suppress them all the time, but did not always succeed.
This often made him difficult to live with.
Unlike his emotions, his interests were boundless, and unconstrained; he enjoyed almost everything.
He loved to let the tension build up before he introduced you to a new topic. He explored the realms of fantasy, created new worlds and was very professional in his timing to reveal the extraordinary.
In his desk he had a drawer that was always locked; it contained his latest secrets.
He allowed you to his room, where you would never enter without his permission.
“Look, it is in that drawer”, he would say. “It is marvelous, you won't believe that such a thing is possible”.
The smell of pipe tobacco, the green ink stains on the desktop, illuminated by a bizarre wrought-iron lamp, which apart from the subdued light, radiated a Gothic mystique, created a very special atmosphere.
He enjoyed the rising tension and a subtle smile appeared around the corners of his mouth.
But if one thought to be introduced to this particular secret right now, you would be mistaken.
In the expectant silence the ticking of the clock was something like the countdown of a rocket launch. And finally, at the pinnacle of suspense, the drawer was ceremoniously opened and a beautiful wooden box appeared.
However, before opening it, he began to talk about gravity; how special it was and that nobody really understood this force. And although it seemed so normal; that when you let something drop, it falls down, in reality it “ is not necessarily so”.

In the box there was a copper gyroscope, the slender axis of a thin metal disc shaped into two circles, like a classic sundial. At the bottom there was a small metal button with a hole that allowed you to put the gyroscope on a large needle.

The tripod with the needle was placed on the desk and the fairly heavy gyroscope was put on top of the point.
And that was not possible. Whatever you tried, the gyroscope fell from the needle and left a dent in the felt covered desk.
Gravity remained the dominant force until.... you pulled a fine string that was wrapped around the disc and made the disk spin very fast.
Then the miracle appeared.
The gyroscope not only stayed on top of the point, but you could put it at almost any angle against the needle. The laws of gravity had disappeared.
A heavy gyroscope, skewed on an angle on top of a vertical needle in space that remained fixed in its position, defied everything that had been certain until then.
The gyroscope was returned to the box and the drawer closed again.
What would come out next time?
Something electric or something with light? You never knew. You just had to wait until that smile appeared and the tension was there again.

How many boxes and how many drawers are there in our lives?
How much surprise and tension can we experience?
A lot, but that smile must be there.
There is so much beauty and everything is so exciting, that it's quite incredible that all those beautiful things so often remain unknown.
It's good to realize that everything is just right there for us. But first, try to let go of all your certainties, because the fear of uncertainty is the source of prejudice.
The desire for certainty is nothing more than a baseless obfuscation of reality. Without certainties and prejudices, everything becomes new and clear. Yet, thinking broadly with an open mind is not enough. You also have to offer feelings some generous space.

Feelings do not exist; they emerge.
In every situation feelings emerge, which are quite different for each individual. What is pleasant and beautiful for one person can be disastrous for the other.
One situation can generate thousands of different feelings, none of which are material, but they are real and have great power.

Because you can't grab or measure them, your feelings will take you outside the realm of logic, in which everything should be measurable and predictable. And that is threatening to many.
For my grandfather, there was no prejudice in the logic of the scientific world and this open-mindedness made him special. But he couldn't cope with the insecurity of his feelings, so he always missed the real essential .

Certainties do not exist, but are only created by the pressure of serious limitations to our sense of reality.
On 17 December 1903, the Wright brothers made their first flight of 59 seconds over a distance of 260 meters. Now, more than a hundred years later, a lot has happened and flying has been fully accepted as normal behavior; we now fly around all over the place.
On 27 September 1905 Einstein published his article about the theory of relativity in the 'Annalen der Physik'. Again, more than a hundred years later, much has happened in thinking about space, time and matter with the result that certainties in this sphere no longer exist; but everything is relative and this fact has become a very threatening mindset for many.

In every situation so-called certainties, that are totally different for each person, arise.
Because we feel that every personal certainty should be the truth, these 'certainties' are being guarded frenetically. These different certainties are often the source of conflicts and wars.
When the molecular structure of antibodies became known in my field of immunology, these proteins turned out to have millions of different forms. The certainty of that time was that each protein was recorded in its own gene on the DNA. That is why millions of genes had to be present for all those antibodies. But then you needed thousands of kilometers of DNA just to make antibodies, and that was impossible.
The segment of DNA for making antibodies is very small, so at conferences everyone was furious with each other and defended his or her vision as the (only) truth.
Later, when it became clear how such a small piece of DNA could form so many different proteins, the peace returned and the old certainties turned out to be outdated by the new reality.

My grandfather taught me to follow new developments with an open mind. And to accept that I can only see a small part of reality and that therefore my certainties of today are likely to be outdated tomorrow.

What I have taught myself is to have an eye for the efficacy of the non-material forces, which are reflected in the world of feelings. Beauty, loneliness and such concepts are not a noncommittal encore of life, but an essential part of our existence.
You are invited to join me in the world of the emotional DNA; but that is only possible if you leave your current certainties and prejudices behind.
Give space to the mechanism of the way in which feelings control our health, and experience that ‘mind over matter’ can become visible in molecular biology.

1

Feelings

When we talk about our feelings, we know exactly what we are talking about. But if we want to know how they emerge and where they come from and what they do to us, then we're not so sure. For many people, feelings are like a fog that flashes through our body.

But is that true?

Feelings are linked to a rock-solid biochemistry that has an enormous impact on our functioning. Not functioning at a vague metaphysical level, but directly on the ins and outs of the cells in our body, up to and including the use of DNA by those cells.

Feelings direct a huge number of vital processes that are not only related to our health, but also have an impact on our lives and well-being; including our lifespan.

How seriously do we take the influence of feelings and what significance do these have in our lives?

In Western culture rational thought plays a very dominant role and the influence of feelings is not taken too seriously. Descartes' statement, 'cogito ergo sum', which means 'I think therefore I am', resonates throughout our world. In addition to Descartes, Plato also caused considerable damage. He confirmed the theory that body and mind can be separated and allocated rational thought, in the form of the Logos, the dominant position. He divided feelings into male, 'Thymos', like bravery , and female feelings, 'Eros' as in sensuality.

Eros is now only associated with a small part of the total female feelings. But this narrow segment of Eros is highly appreciated. There is little room or recognition for male feelings and the time of 'men don't cry' is not far behind us, if it's behind us at all.

The division into body and mind and the further division of mind with the domination of thought (the logos) and the subordinate position of feelings, is deeply rooted. This image is so well established that a different approach not only encounters wide spread prejudice, but also provokes a great deal of aggression.

But why are feelings so undervalued, if not ignored, in our culture?

Because the logos is only capable of dealing with material, measurable and tangible objects; it is reluctant to become involved in non-material, non-measurable or abstract processes.

Feelings do not exist, but emerge!

They are not tangible, but they nevertheless are real and can be enormously powerful. Feelings emerge from the interaction of material matters, resulting in a nonmaterial force that cannot be recognized in its isolated components. In the interaction between people, for example, feelings that are generated, have a tremendous driving force but are not tangible or measurable. In a positive interaction this is called love and in a negative one hatred. Strong forces emerge through love or hatred, these are non-material but very real.

Because feelings in their isolated form do not exist, they fall outside the logos' terrain. If a culture is primarily rational in structure, there is little room for feelings. Their strength is indeed experienced, but difficult to be quantified in a dominant logical world; so they are habitually avoided or denied.

It is always difficult to set aside prejudices and it is therefore easier to analyze the effect of feelings in a neutral context. To exclude all psychological and other variables, we will look at the feelings of rats and the influence on their existence.

The nice thing about rodents is that they are genetically quite healthy and even if they are inbred they don't display terrible abnormalities. You can breed large numbers of animals that are genetically identical. There is a type of rat with the euphonious name Sprague Dawley and the feeling we are going to study through them is loneliness.

Rats are very social animals and live in groups. What happens if everything stays the same for these animals but only the accommodation changes? Instead of placing them in groups, they are placed in a cage on their own. The rest of the care remains unchanged and at Hilton level.

Experiencing loneliness has an incredibly great effect on these animals, so great that it is almost impossible to comprehend.

In these rats, the females have a strong genetic predisposition to breast cancer. Under normal circumstances a percentage of the females will, after a certain period of time, spontaneously develop breast cancer that does not metastasize. If the females were not housed in groups but instead placed in a cage, the loneliness through this social isolation proved to have a direct effect on the development of breast cancer. After a similar period, a much higher number of the isolated females did not have one small tumor, but several tumor hot spots. The total size of the tumor was eighty-four times as large and, in addition, a large number became malignant and metastasized (1) .
How does loneliness make tumors larger and malignant?

The short answer is that this sense of loneliness changes the use of DNA. Genes that make growth factors for blood vessels are stimulated by loneliness. This gives the tumor more blood vessels and therefore more oxygen and nutrition, resulting in tumor growth. Similarly, the genes for certain adhesion proteins are activated, which allows the tumor metastasize.

The long answer to the question: ‘what controls the relationship between feeling and DNA’ will become clear in the upcoming chapters.

Not only is the progression of breast cancer different in our rats, there's a lot more happening at the same time. If you want to delve into scientific literature, the following website makes an excellent entry point: http://www.ncbi.nlm.nih.gov/pubmed/. Look for: ‘social isolation', and find over 26.000 related articles. If you limit this search to only the effects in rats, you will still have 1956 articles left to explore. The differences that are found, cover almost every area.

For example, the brain development and activity of important structures in the area that we call ‘between the ears', such as thalamus and hippocampus, are different in relation to solitude. (2) Many more brain functions change, not only at the level of neurotransmitters and their receptors, but also in hormone production, metabolic activity and addiction sensitivity. The development of the cortex, the part where thinking and awareness are located, is also influenced, as is the ability to adapt to changed circumstances. All these changes in the brain are in turn reflected in behavior and sensitivity to mental disorders. (3)

To further elaborate on the effect of the ‘solitude emotion,’ it can be seen that the heart rate frequency and the occurrence of high blood pressure are directly affected. (4) but the structure of the liver also changes (5) whilst breast development changes in females (6) and the immune system’s activity in the animals decreases. (7) This, in turn, affects wound healing. In general, conditions are getting worse for animals in isolation. (8) However, a ‘plaster on the wound’ is possible . Although the animal remains isolated, the ability to heal wounds is considerably better if you make the isolation more bearable by, for instance, adding extra nesting material. (9)

It will be clear that this sense of loneliness has an overwhelming influence on the development, well-being and behavior of these creatures. But what about man?

As mentioned above, wound healing in rats is influenced by environmental factors. Let us look at this aspect in humans.

Once upon a time there was a boy who was often ill and had a lot of pain. From his bed he looked out at a beautiful tree and when he was looking at that tree for a while it seemed as if he was suffering less pain. The tree became a support and refuge for him. Later, as a surgeon, he worked in a hospital ward with eight patient rooms. Four of those rooms looked out onto a blind wall and four had views on a park with large trees.

From his previous experience with the tree, he was curious whether the healing process of the patients was influenced by the view. For nine years, he collected the data from patients all of whom had undergone the same operation. To everyone's surprise, it turned out that the patients in the rooms with the view on the trees received significantly fewer painkillers and tranquilizers, had fewer other complaints such as headaches and nausea, and had to stay in hospital for a shorter period of time. (10)

When we talk about the influence of loneliness, it is clear that something different from just being alone is at play. Many people are happy to be alone and therefore experience no stress. Alone but not lonely, is something quite different from a social isolation, that is perceived as negative. In the latter case, all the stress mechanisms in the body will be activated and its use of DNA will be changed. But what do we have to expect in case of change in our DNA usage? All this will be further elaborated in the forthcoming chapters.

It is simply the case that we all started as one cell and when cells are divided, the DNA is copied but remains the same. Therefore DNA is the same in all our cells; and there are more than a few cells in our body; a number with fourteen zeros.

However, these hundreds of trillions of cells have all kinds of different functions, and each type of cell therefore uses a different set of genes. Although cells possess the information for all functions, to function specifically they need to switch genes on or off in order to obtain the desired effect. There are a number of mechanisms available that allow the cell to turn functions on and off. A very important mechanism is the use of transcription factors. These proteins are a type of DNA switches that recognize specific DNA sequences adjacent to a gene. After bonding to this sequence, they regulate the use of that gene. This specific sequence for a transcription factor is placed not just next to one gene, but next to hundreds of genes. And when a transcription factor becomes active in a cell, many functions change at once.

Now it appears that feelings and emotions start from a complex mix of brain processes, that lead to the activation or inhibition of transcription factors and thus change a lot of functions at the same time.

If we stay with the feeling of loneliness, then this feeling will, through the brain, hormones, etcetera, eventually result in activation of the transcription factors. But how can we see that?

In one study, the gene use of certain cells has been measured in two similar groups of people. The only difference was that one group was socially isolated and felt this as loneliness. Via a smart DNA chip it can be seen which genes are used by a cell. If we then analyze these data with a special computer program, the differences can be listed. The genes that go up in one group are shown in grey and those that go down in white. You will then get the following result, see figure 1.

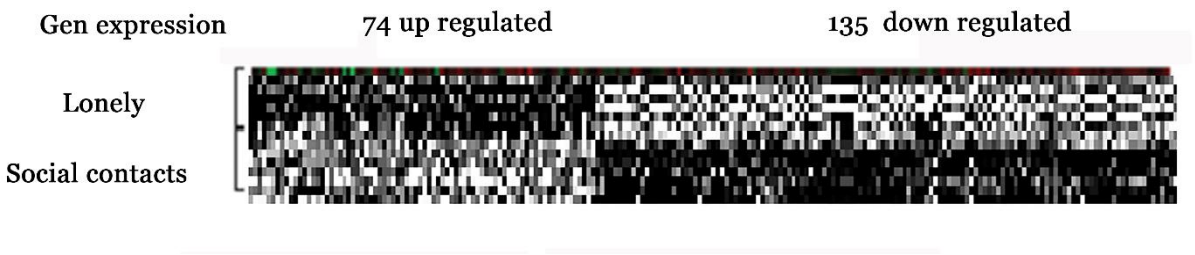

Figure 1. *Differences in gene expression among people in social isolation. White: lower expression genes, grey: genes with higher expression*

In total, 209 differences in gene expression were measured. Each gene has a special sequence next to it, to which a transcription factor can be attached. By looking at this sequence you can see which transcription factors are activated or inhibited for all those 209 genes.

As a result, it emerges that loneliness has a strong effect on the immune system, among other things. The transcription factor that inhibits defense functions, is reduced with loneliness and the factor that stimulates defense functions is increased. This causes the immune system to become unbalanced. You can compare this to a car with rickety brakes, in which the accelerator pedal often becomes stuck. Loneliness increases the risk of developing inflammatory diseases, such as auto-immune diseases. And the course of cancer is also influenced, among other things. (11)

The effect of social isolation, experienced as loneliness, is enormous and deeply interferes with the use of DNA. But what about all the other feelings, and do positive feelings have a different effect than negative ones?

A brilliant answer to this question can be obtained from the research on telomeres. These are the ends of each chromosome. In popular parlance, a telomere is deemed to be similar to the plastic cover at the end of a shoelace. If this breaks down, the frayed ends quickly become unusable. The length of the telomeres is extremely important in cell aging, and thus the survival and functioning of a cell. If a telomere has become too short, the cell dies, but there is also a mechanism that causes telomeres to become longer again after shortening.

The discovery of the existence of telomeres and how their length can be influenced, received the Nobel Prize for Medicine in 2009.

It turns out that feelings are enormously influential in this process. Chronic stress causes the telomeres to speed up the shortening, resulting in cell's aging and that results in many years shorter life expectancy. (12) After this particular influence of chronic stress was discovered, the researchers began to study the other side of the coin. If chronic stress is so bad, what could be the effect of inner peace, for example, through mindfulness? (13) An extensive study has clearly demonstrated that mindfulness has a direct positive effect on the length of telomeres and thus counteracts cell aging and related processes. (14)

In addition to the influence of our feelings on telomeres, many different effects have been described. The search term ‘psychological stress' on the Pub Med website contains 144,548 articles in the scientific literature. This information does show that psychological stress is far from beneficial to health. Stress is a real ‘stealth assassin’, and it is astonishing that this phenomenon has been accepted in our society in such cavalier manner. The answer to the question: ‘How are you doing' is often: ‘busy, busy, busy'; mostly said with pride, whilst a poorer attitude to life is hardly possible and people should more likely be ashamed of this attitude. Psychological stress, but also psychological intervention, can have a direct effect on the course of a disease like breast cancer. (15) Although this relationship between mental condition and illness is felt by many, the common belief that body and mind are separated is so strongly embedded in our culture, that people often treat their mental health very carelessly, if they are aware of it at all.

As if the misery caused by chronic stress were not enough, the influence goes even far beyond the present, namely to the next generation. Here we enter an amazing field, which has only recently been discovered. It is called epigenetics. It is remarkable enough that feelings can influence the activity of genes, but now it has become clear that, for example, stress can permanently block genes. This is brought about by a small chemical reaction, in which a methyl group is bound to the DNA at a specific location, with the result that this gene can be blocked for life. Although the mechanism is not yet fully known, it is clear that this blocking can be passed on to the next generation and even to the third generation. An example for this is that rats growing up in isolation have a decreased activity of an important hormone in the brain. The offspring from such rats with low levels of this hormone, which, even when raised socially and lovingly, will still turn out to have the same defects caused by the loneliness of the parents. (16)

The abundance of scientific articles on the influence of both positive and negative feelings in animals and humans undeniably reveal the fact that our feelings and emotions profoundly influence our physical functioning, up to the level of our DNA, and even can, through epigenetic mechanisms, echo into the next generation(s).

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Burnout

Just like many things and ideas, the concept of illness has been perceived differently in the course of time.
The era that sickness was a punishment of the gods for committed sins, has been behind us for some time now.
Around 1900 diseases were strongly dominated by infectious diseases, because of which a clear and easily definable situation arose. The pathogen was a bacterium or virus that came from outside, the diagnosis was unequivocal and the associated fever and malaise were undeniable signs of being ill. This gave rise to the idea that the cause of a disease can be clearly defined, and also that the symptoms must be measurable.
This image was reasonably applicable to the situation a century ago, but in the current situation this view often conflicts with reality. By reducing infectious diseases, a situation is now created in which the cause of a disease is often complex, making the diagnosis difficult to make, and therefore no unequivocal treatment is available. Work pressure, stress, lifestyle, heavily processed food, pollution, etcetera can cause a wide range of concrete diseases, with a variety of phenomena that are often not even recognized as illnesses.
But why is it so difficult to see that the pattern of pathogens has changed dramatically? Social structures have become concrete pathogens and have largely displaced bacteria. The idea that a management structure, or a political decision on market forces in health care, will upset your immune system and result in a chronic malaise, is not always understood by everyone. In fact, it evokes aggression. Surely a political decision cannot increase your IL-6 level in the blood, with as a result that in your brain the sleep center is activated with chronic fatigue as a result. Isn't that clear nonsense? To make things worse, I would like to say that distrust is also an important pathogen.

The confidence gap

The enormous increase in today's lifestyle diseases, in which already half of the population has some kind of chronic condition, cannot, of course, be explained by one simple fact. However, it is clear that all these inflammatory diseases, with the associated fatigue, burnout, pain and depression, have a clear relationship with psychological stress. As a result, the gene use on the DNA is chronically misdirected, with all the consequences that entails. There are

many causes for the increased psychological stress, but an important reason is the confidence gap.

The longing for certainties and control has been completely eroded lately, with the result that everything now has to be protocoled and administered, while there is no longer a basic trust. Through all these rules and protocols one is squeezed into an unnatural straitjacket, whereby one loses the essential freedom to decide for oneself in a given situation.

As a result, the doctor spends more than half of his time on administration, and if he deviates from the protocol when treating a patient, he is either not reimbursed or he might even lose his license . The student as well is suffocated by rules and study credits, and instead of his scientific development, he is trapped in a network of administrative protocols. By restricting one's own freedom and responsibility, and replacing this by distrust and control, a pathogenic chronic stress arises.

It is not so long ago that nobody knew the concept of burnout, while now a burnout epidemic has arisen. The phenomenon of burnout is strongly present in specific groups such as doctors, nursing staff and students, but it is also present in a broader sense. The millennial's have been severely affected by this new phenomenon, but depending on the management system, burnout also appears more and more on the workplace.

Management models can vary greatly, with a strong desire for control as well, and often trust is no longer the standard starting point.

Should employees be accountable or take responsibility? Quarterly figures and short-term planning often take precedence over actual interests. Must everything be as efficient and inexpensive as possible, or is there also appreciation for craftsmanship and quality? Without trust and personal responsibility, job satisfaction is low, stress will increase and can eventually lead to a burnout.

Although burnout is in principle nothing more than chronic stress, the question arises as to what makes it something so special?

The answer lies in the nature of the stressor. The usual stressors that influence your life and lead to chronic stress, are mainly of a personal nature. No matter how severe such relationship problems, illnesses etcetera are, you can either do something about them, or try to accept them; but they are your stressors and you have to learn to deal with them. Burnout is not about personal stressors, but about social stressors. This makes you the victim of a stressor, on which you can't exert any influence yourself, but still has a huge disastrous impact on your life.

Now take the current student as an example. When I started studying, there was no rigid curriculum. For four years you paid two hundred guilders tuition fees, which meant that you were enrolled forever. You had to take a number of practica and exams for your bachelor, and then a number of exams for your masters. Et voilà there was, like a rabbit in the tall hat, the brand-new doctoral student, regardless of how he had completed the program. I myself remained childlike for a long time and woke up late, but that didn't bother anyone except myself. But now everything is logged to the millimeter. If you don't have enough points in the spring of the first year, you are actually forced to end your study. So, an external stressor based on distrust, can influence your whole life. You have to enter the straitjacket of the protocol that doesn't suit you at all, which you cannot control yourself. These rigid social structures, which literally ruin both education and the later working environment, have recently become so dominant that there is now a burnout epidemic. Many studies have been carried out on this subject, all of which indeed show that a structurally negative working environment can lead to a burnout. (147). This is also reflected in the definition of burnout used by the World Health Organization (WHO).

"Burnout is a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed".

The powerlessness and lack of control over these social stressors make burnout an even more serious form of chronic stress.

Burnout as an inflammatory disease

One of the many aspects of chronic stress, is modifying the activity of transcription factors causing a change of gene expression on the DNA. This also includes the transcription factor NF kappa B, which plays a very important role in inflammatory processes. As we have seen in chapter 8, the immune system is very complex and can be seen as a large yin-yang event, in which hundreds of factors balance each other in various ways to achieve a very delicate equilibrium. Not only is the chosen type of defense very important, but also the strength of the reaction, and the location in the body. If, for example, a bacterial infection in a muscle is dealt with aggressively, and scar tissue develops afterwards, this is not a problem. But with the same approach in the eye, one would go blind. Not only is an inflammatory reaction very complex, but it becomes even more complicated, because these inflammatory factors also interact with the brain. If you have a severe flu, you're exhausted, you can't tolerate any sounds or light, you've lost your appetite, and you've got a nasty fever. You might also get a

banging headache, and when you feel better in the end, you're very weak with little strength in your muscles. All these symptoms are caused by the interaction of the immune system with the brain.

Every infection has its own special combination of inflammatory factors, which results in a recognizable disease pattern. Measles have red spots, and chicken pox or shingles also have their own recognizable symptoms. This makes it easy to diagnose infectious diseases. But Pandora's immunological box is filled with hundreds of factors, and if it is opened in case of chronic stress, the most diverse combinations can occur. As a result, the effects of chronic stress are individually very different and unpredictable. One person is dominated by pain and anxiety, while another is dominated by fatigue and depression. Where there is clarity in viral or bacterial infections, there is an unpredictable combination of symptoms with chronic stress. The effects of these inflammatory profiles are quite variable, but can be summarized as malaise. This "malaise" covers a wide range of conditions, often hidden under the heading of: "somatically insufficiently explained physical complaints", which are subject to constant bickering as to whether they are "diseases" or not. This confusion is the sad legacy of Descartes, who states that only logic would dominate our existence and feelings do not matter.

It is possible to measure all kinds of inflammatory factors in the blood, but these only indicate that there is a changed inflammatory profile, with no insight into where and how strong the inflammation occurs. What is really going on with burnout or ME/CFS?

If you look up the wiki definition of ME, it doesn't make more sense, but you will understand that it is serious.

Myalgic encephalomyelitis (ME) means inflammation of the spinal cord (myelitis) and/or brain (encephalitis) associated with muscle pain (myalgia). Patients experience disabling exercise-related physical and mental fatigue, muscle pain, flu-like malaise, abnormal exhaustion not resolved by sleep, and other symptoms including loss of concentration and short-term memory, sleep disturbance, dyslexia, balance disturbance, sensitivity to light and noise as well as alcohol intolerance, mood swings, sight and stomach problems - symptoms vary and fluctuate.

Chronic fatigue syndrome (CFS) cannot really be distinguished from ME, and is therefore summarized as ME/CFS. Burnout falls into the same category of misery.

According to Wiki: *Burnout is a physiological disorder in which the patient is emotionally and physically exhausted and can perform little or nothing.*

Many of these symptoms can be explained by the immune system's interaction with the brain, but how can you tell that there are inflammations in the brain?

Just a little scientific background. The immune cells, involved in inflammations in the brain, are called astrocytes and microglia cells. When these cells are activated by inflammatory factors, they express a certain receptor on their surface, the 18 kD Translocator Protein. If you now make a particular substance that can bind specifically to this receptor, and have labelled it as such that it becomes visible in a PET scan, you can distinguish between active and inactive immune cells in the brain. In this way it has been shown that ME/CFS has an inflammation in different vital parts of the brain. (148).

So it is indeed between the ears, because these inflammations were demonstrable in many places in the brain, but were also strongly present in the limbic system, where the feelings reside, such as the thalamus, amygdala and hippocampus. The intensity of inflammation in these areas directly correlated with the degree of cognitive impairment, depression, fatigue, pain sensitivity and nervousness.

When looking at the blood of these patients, there are some differences seen in inflammatory factors (e.g. gamma interferon), but no unequivocal significant picture emerges. Thus, blood diagnostics are not the right way forward, and this explains why a simple standard diagnosis can only lead to the conclusion that physical symptoms are somatically insufficiently explained.

Burnout also measures strong changes in brain structure and function. (149).

Changes occur not only in the individual areas of the brain, but also in the cooperation between those areas. The functional connectivity between the amygdala and the prefrontal cortex is affected, and this cooperation is so important for the correct processing of emotions. (150)

In case of burnout, but also other conditions such as ME/CFS, fibromyalgia and other similar conditions, it is difficult to immediately find a measurable cause. There is a lot wrong and the malaise is very heterogeneous in composition. A kaleidoscopic combination of physical phenomena occurs, making a clear diagnosis impossible. This, combined with a large dose of psychological complaints, means that classic medical thinking about cause and effect of diseases, is in serious trouble. Because the classical image of diseases, which used to be mainly determined by infectious diseases, is still strongly dominated, the idea that personal and social living conditions are a direct source of diseases is often not accepted. Therefore, the solution that is commonly put forward is too simple; if there are no clear physical and

measurable causes, these conditions cannot be real diseases, but rather something vague between the ears. If the symptoms last for years, then the lack of understanding is complete. For this reason, the burnout field is too often searched for a simple explanation. There is chronic stress, so after a while the stress system will be exhausted. The adrenal gland, an important producer of stress hormones, would become overtired. However, this is a bit too short-sighted, and after analysis of many studies one can conclude that this "adrenal fatigue" as such, does not exist. (151) but that there is a disruption of the adrenal function.

In the case of burnout, one should not look for single measurable facts, but rather think in terms of a disturbed interaction of several vital areas. The altered gene expression patterns, induced by chronic stress, affect the interaction between the immune system, brain structures and functions, metabolism, the HPA axis, with all its stress hormones, epigenetics and on top of that the intestinal flora, the microbiome.

To illustrate the true complexity of burnout, here's a boring but impressive list of the minimum things that go wrong. (152)

In the **pituitary gland**: Oxytocin (the feel good hormone) and GHRH (growth hormone) are lowered.

CRH, POMC and ACTH (stress hormones) have been increased.

The negative feedback of stress hormones on their own production is disturbed, which disrupts the return to the resting state.

The **adrenal gland**: *hyperactive* in the production of cortisol, which is also too slowly broken down by the enzyme 11-beta HSD2. *Hypo-active* due to deregulation of several systems, such as insufficient production of adrenaline and nor-epinephrine for the feedback regulation of ACTH.

In the **thyroid gland**: the inactive thyroid hormone T4 must be converted into active T3, the hormone that drives the metabolism. This conversion from T4 to T3 by the enzyme 5′-deiodinase, is inhibited.

In the **pineal gland**: the production of the sleep hormone melatonin is reduced.

The enzyme tyrosine hydroxylase is reduced. This reduces the formation of L-dopa, which is the precursor for the important neurotransmitters dopamine, adrenaline and nor-epinephrine.

In the **immune system**: inflammatory factors are increased such as IL-1, IL-6, interferon and TNF-alpha. Anti-inflammatory factors such as IL-10 have been reduced.

In the **autonomic nervous system**: the balance between the sympathetic and parasympathetic nervous system is disturbed. The sympathetic system, which activates organs and bodily

functions, is overactive, while the parasympathetic system, which calms everything down and establishes a healthy balance, is inhibited.

In the **central nervous system**: structural and functional changes. Differences have been measured with functional MRI, in several brain areas, such as amygdala, hippocampus, prefrontal cortex, nucleus caudatus and putamen. Not only do functions change, but there are also differences in the volume of these brain regions.

Neuro-inflammation; inflammation is measured in several areas, especially in the limbic system. *Growth factors*; the growth and maintenance factors BDNF and GDNF, which are essential for the brain, have been reduced, resulting in increased nerve degradation and mortality.

Looking at this list of changes, it is clear why burnout has such a wide variety of physical and psychological symptoms. Each complaint is the result of a combination of many factors, which differ from one individual to another. Some complaints can still be explained in a reasonable way, such as fatigue for example. This is partly due to the interaction of immunological factors such as IL-6, with the different areas in the brain and the brain stem, that are involved in sleep and fatigue. This fatigue is thus independent of effort. Another way to explain fatigue is from the changed thyroid activity. Because the pineal gland also makes too little melatonin, the sleep mechanism is disturbed, which makes you sleep badly and you become even more tired.

If we want to explain other complaints, such as concentration disorders, the it becomes really complicated. We then have to combine the interactions and activities of many brain areas, that have been functionally and structurally altered by inflammatory processes, and lack of growth factors, such as BDNF.

As if it were not enough, a severe burnout also affects the enzymes that are involved in blocking genes, and this can result in a large number of epigenetic changes in the DNA. The many unfavorable changes are also permanently anchored in the DNA. The gene of the very important nerve maintenance factor (BDNF) is partially blocked, as is the important thyroid enzyme, tyrosine hydroxylase (TH). The connection between nerve cells is formed by the synapses, that ensure whether the signal is passed on. All kinds of important components in the synapses are epigenetically influenced, causing nerves to function differently on a permanent basis.

The chronic stress of burnout not only temporarily changes the gene expression on the DNA, causing a wide range of problems, but can also anchor this misery in the DNA through

epigenetic processes. This could be one of the reasons why a burnout takes so long, and can even lead to permanent damage. (153)
Although not simple, epigenetic processes can still be reversed. The knowledge about removing epigenetic blockages is still in its infancy, but it is clear that certain vitamins, cofactors and other specific compounds can have a great effect, from the point of view of nutrition. (154)

Burnout, what to do?

The real solution is very simple, but almost impossible.
Back to the social structures based on trust and personal responsibility.
From all the definitions concerning burnout, the concept of work-related stress always emerges. Organizations and companies have developed more and more structures in recent years, in which the human values of the employee, such as contribution, responsibility, quality and job satisfaction, have been replaced by suffocating control bureaucracy, regulations and protocols, with the sole aim of financial gain. These developments, which deprive people of their dignity, are the real reasons behind the burnout phenomenon.
The solution for the burnout patient, by taking some rest and not working temporarily, does not have any real impact, because the cause lies outside himself. Another major problem that has often not given enough attention to, is the conditioning that has occurred. In a conditioned reaction, an irrelevant perception is combined with a physical reaction. The classic example is the Pavlov reaction, in which a dog is conditioned in such a way, that he starts producing saliva at the sound of a bell. The burnout patient associates all kinds of random environmental factors with the work stress, and then triggers the physical stress reaction. For example, opening a random e-mail, may be associated with work stress, or cycling through a particular street. Such an emotional association leads to a physical reaction, as a result of which, among other things, the IL-6 concentration in the blood may have risen tenfold after an hour and a half, resulting in a feeling of fatigue. (155)
So by a number of daily conditioned emotional associations, you may literally feel continuously burned down.

As long as there are no social changes, burnout will remain a major problem. The person who is affected, can either choose to fight the symptoms, or he can see this as a signal to change his life in a drastic way.

21

Feelings don’t exist, they emerge

Aristotle was a wise man who said, "The whole is more than the sum of its parts”.

But in order to be able to understand a complex system, it is an effective approach to first divide the whole into parts, and then study them in more detail. In a very complex system, these parts are divided over and over again, until a level is reached that ultimately can be analyzed. This reductionist approach assumes that a complex entity can be retraced to a collection of smaller, fundamental entities. Contemporary science is very reductionistic and, with this approach, very successful. But this actually comes down to the statement: 'The whole is the sum of its parts'.

But what about Aristotle?

If we look at medical science, how does such a reductionist approach work?

Starting from biology, we move on to biochemistry and then to chemistry, which in turn can be reduced to physics, and through mathematics we arrive at the level of logic.

Here we have arrived at Plato's logos and Descartes' thinking. Logos is the rationality, which distinguishes us from the animal. In addition, Plato had divided human emotions into male emotions, Thymos, and female emotions, Eros. He compared man's soul to a chariot, towed by two horses. Rational thinking is the charioteer, and the two feelings, Thymos and Eros, are the horses that are controlled by Logos. In the seventeenth century, Descartes further upgraded logical thinking by saying: 'I think therefore I am'.

But are Plato's emotions so subordinate to Logos and not relevant to Descartes' approach? You only have to look around to see that Logos, in human action, soon loses from Eros. And there is no Logos at all in politics. Here, Thymos dominates, in the form of emotions such as power and pride, but often Eros puts an end to the political career.

With reductionist thinking, it is easy to reduce a house to bricks, cement and all other building components. But all the components put together, do not create a house. The form ultimately determines the house, or the spatial orientation of all the elements. This spatial orientation cannot be found in the isolated elements.

Another wonderful example is a swarm of birds. The reductionist unit of a swarm is the individual bird, but with this single bird it is impossible to study the mechanism of the swarm. It is the dynamic interaction of the birds that together produce the swarm, as can be seen in figure 45.

The term for this phenomenon is emergent. Emergence means that a system exhibits characteristics that cannot be found in its constituent parts, but that this new characteristic is created by the interaction of the parts.

Figure 45. *Birds swarming*

The best example of emergence is life. It is the dynamic interaction between all the cells and molecules that generate this new entity, life. As soon as the dynamics of these interactions stop, death occurs, and it becomes painfully clear that life is not only a lot of cells and molecules. A reductionist approach to life generates knowledge about the constituent components, such as organs, blood, and so on. But with this step, the essential understanding of what life is about is lost, because the essence of life is only in the dynamic interaction. In reductionist thinking, you go back one step at a time, and lose parts of the essential overview. When studying emergent phenomena, you have to take a step further, and then out of nowhere completely new things appear. Life is as concrete and abstract as a dance. The nice thing about reductionism is that you get deeper and deeper into the kind of thinking that is

dominated by Logos. If the thinking goes in the opposite direction, the influence of Logos becomes less and less, because in the dynamic interactions there are more degrees of freedom, that can change spontaneously, without cause and effect, and therefore go beyond the Logos.

Our thinking has been marinated in reductionism and false certainties for centuries. That is why Einstein's theory of relativity, in which he says that everything is relative, is difficult to understand. It shows that reality is based on dynamic interactions between the observer and the observed, where there are no certainties and everything is relative. If you take another step further in the understanding of reality, you come into the field of quantum mechanics. There, matter is nothing but probabilities between dynamic interactions of undulating fields, and there is little left of Logos. Most symptoms occur spontaneously, without any cause. Even for Einstein this way of thinking was no longer acceptable, because of his religion he could not separate himself from the cause-and-effect principle. This gave rise to his famous statement: 'God does not play dice.'

If you stop classical reductionist thinking and make room for what appears when you focus on the dynamic interactions between components, you will end up in a beautiful world. Then the things that emerge, are of a totally different order than the simple way by which we describe matter. These events however are very real, even if they are not tangible; they are emergent processes such as life, dance and even gravity.

Recently, the Dutch physicist Erik Verlinde postulated that gravity as such does not exist, but is an emergent phenomenon that arises from special quantum-mechanical interactions. (156) His reasoning is beautiful and very convincing, but one shouldn't think rigidly and logically, not to miss everything of this vision that elevates gravity over matter. It comes down to the fact that material particles, outside space and time, are entangled with each other. Through this connection outside space and time, entanglement induces a higher order of organization of matter. This higher organization causes a change in entropy, and the force that arises from altered entropy is gravity. Gravity does not exist, but emerges from the interaction of matter at a higher level. The existence of entanglement, in which information is exchanged between particles, outside space and time, has been proven beyond doubt at thousands of times. That information not only goes faster than the speed of light, but is instantaneously, without time being involved. This was total horror for Einstein, because it completely undermines logical thinking, based on the mechanism of cause and effect.
A pity for Einstein, but entanglement is real. It turns out that the Logos of Plato is usable in only a very limited area of nature. Einstein's theory of relativity already elevates thinking

above the Logos, and in quantum mechanics this way of thinking is even more complex, and reduces relativity to only child's play. Rational thinking with its logic, is too primitive to describe reality.

What are the consequences, if we start at the level of logical thinking and take the reductionist route from there? Or when we go the other way, in the emergent holistic direction, in which the combination of the parts unexpectedly creates new, immaterial, but very real forces which are the 'more' of the sum of the parts?

The current medical science is very reductionist and even goes so far, that a sharp separation has been created between the specialisms. This is implemented to the extent that every organ or system in a hospital is also housed at separate locations, where communication between these departments often does not deserve the main prize. A holistic integration of symptoms and disorders is therefore rare.

Just a little bit of Aristotle. It is clear that the whole is more than the sum of things. That 'more' is localized in the dynamic interaction of the components. These interactions are very concrete and produce forces, however, in their isolated form they are not tangible for the reductionist thinker. We call that abstractions, the shape of a house as such is not tangible. The dynamic interaction between two people has form and power. In a positive sense we call this love, in a negative sense we call it hatred. Love and hate are concrete phenomena and can generate great forces, but they are not objects and they are not even matter.

In medicine, attention is mainly focused in a reductionist way on the individual components, and little on the dynamic interactions between all these systems. What we then see is that in the field of these interactions, processes and forces arise, which are not, or hardly, recognized in reductionist or classical medicine.

If we take an emergent or holistic view of diseases, we need to go further than just looking at the functioning of the organs, the concentration of hormones, and so on. These are indeed necessary ingredients to gain insight into the current state of the patient, but by staying at this level, a lot of essential things can be missed.

These are the biological phenomena that originate from the dynamic interaction of the various physical components, but are not tangible, real and powerful. These are feelings, and they appear in an interaction between biochemical systems.

Feelings don't exist, they emerge!

Pain does not exist, but is a result of the complex interaction of the receptors in tissues, the number of nerves involved in pain conduction, the amount of trimers of the ASIC1a receptors in the synapses, the amount of Substance P, the degree of stimulation of GABA receptors, observations from the environment, and so on. Purely reductionistic pain does not exist. Pain is the result of the interaction of many systems and as such it cannot be measured, and is also very influenceable. Fear does not exist, but is the non-measurable result of very many complex interactions, including past experiences. But do pain and anxiety not exist? Depression does not exist either as a localizable or measurable item. It is a very complex interplay, of again very complex interactions between neurotransmitters, metabolism, immune functions, even intestinal flora, but oh, so real and it determines to a large extent the quality of life.

Feelings do not exist in the reductionist sense, because they are not in themselves existing entities; they appear from interactions with other systems, and therefore are emergent. Does that mean that feelings do not exist and have no strength?

That is where the problem lies in the medical world. During two thousand years, reductionist thinking has been applied and the various systems have been identified. The result is fantastic, complex molecules have been unraveled and the most advanced measurements can be done. However, there is also a downside to this process, namely that the holistic approach is being trampled. It even goes so far, that the medical action is protocolized, as if everything is measurable, logical and predictable. Unfortunately, there is no room for feelings in all these protocols. But how bad is that?

If feelings had little meaning, it wouldn't be that bad, but the opposite is true.

Our contact with the outside world goes through the senses and goes first to the limbic system, where via the amygdala every perception is given a value judgement, after which it is linked to all the emotional memories from the past. This results in dynamic interactions between all kinds of parts of the limbic system, with the associated neurotransmitters, and then a feeling emerges from these complex interactions.

Depending on the final feeling that has been formed, the hormone factory in the pituitary goes into operation. It releases a large amount of different hormones which, together with the many nerve circuits, affect the whole body. Apart from the fact that these hormones have their specific activity, they also can start other functions. For example, the hormone cortisol, together with its receptor, forms a transcription factor that controls 20% of our genes on the

DNA. In addition, many other transcription factors change their activity, based on the original feeling. This can lead to epigenetic changes in the DNA, which can have a lifelong effect and even generate an echo that might last up to three generations.

Feelings are dominant in the functioning of our body and are at the basis of our health. The Nobel Prize for Medicine 2009 was given for a study which shows that feelings of stress directly influence the life span of humans, by shortening the telomeres on the DNA. The immune system is in direct contact with the central nervous system, and feelings control the degree of chronic inflammation. Our entire metabolism, up to and including the intestinal flora, is partly controlled by our feelings. Almost all diseases related to western civilization have a strong connection with our feelings.

Because medical thinking remains stuck in the reductionist logic, one underestimates, or even doesn't see, the forces of immaterial, but real, feelings such as pain, loneliness, fear, hope and love. These feelings emerge from the dynamic interaction of the underlying biochemical processes. But while one does not want to recognize the effect of feelings as a serious factor, billions are spent to determine the effect of these feelings. That is the double blind research, which aims to eliminate the effect of feelings on healing, the placebo effect. The interaction between doctor and patient gives rise to feelings, such as hope. These feelings are so important and powerful that they determine the healing process to an important extent. With a good positive conversation, even a peppermint gets a magical power. This placebo effect is very large and gives a percentage contribution to the healing process, which can often exceed fifty percent. (157) Extensive studies have been carried out on this placebo effect, and in any condition, attention and understanding of the situation combined with hope and a positive image, always have an unlikely high effect. The neurobiological mechanism of the placebo effect is approximately the opposite of the stress response. Through the interaction between doctor and patient, large, measurable changes occur in brain activities, stress hormones, endorphins, and so on. (158) As far as the whole placebo effect is concerned, the biggest contribution lies in the quality of the doctor-patient relationship. (159) If the doctor knows that he is giving a placebo, he will be less convincing and the effect will be different. Therefore, all clinical trials are performed double blind, so the doctor does not know whether he is prescribing a placebo or a medicine. Another striking effect is that, when the placebo is very expensive, it has a better effect than a cheaper variant. (160). The placebo effect was also investigated during knee operations, where the pain was caused by arthritis. If only a scoop was used without any further action, the result was the same as when a real operation took

place. (161) As the placebo effect uses components that are also operational in the stress response, the placebo effect is therefore also dependent on the genetics of these components. The genetic background, in terms of sensitivity to the placebo effect, is now partly mapped out. From this it becomes clear that, depending on their genetics, people are more or less sensitive to placebos. (162) It is a pity that in medicine so much effort is being made, not to take into account the effect of feelings according to health, while those feelings are so important.

In the development of science, new insights have constantly arisen, which disprove the certainties of the past and necessitate a new view of reality. Conservatively clinging to the old principles and prejudice is not a fruitful attitude to life.

This enormous development in thinking has been going on for more than a century, and is clearly showing that there are no certainties. Everything is relative and our observations, since quantum mechanics, are expanding beyond the physical material. Also, the virtual world, outside space and time, has become so accessible, that the first applications, in the form of quantum computers, are already being developed.

Give it a try to go further than simple logic, with an open mind to the intangible but real forces that come from feelings. Step over prejudices and don't rush along in today's sickening rat race, but strive for harmony instead of stress and haste.

How to de-stress and improve your quality of life has become clear in all these chapters. It is actually very simple and it costs nothing, but you have to decide for yourself whether or not you are going to do this.

The only advice I would like to give to you is:

Take your agenda and plan yourself for half an hour every day, and don’t let this time be disturbed by anything or anybody. If you don't have time for half an hour, plan for an hour and a half.

Welcome to the world of emotional DNA.

Understand how feelings guide our health and how mind over matter becomes visible in molecular biology.