Biological Information Processing

by

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CONTENTS

Glossary

ACTH	Adrenocorticotropic hormone
BIS	Bio-informative state
BM	Body / Mind
CNS	Central nervous system
CRH	Corticotropic releasing hormone
CO	Consciousness
IL	Interleukin
IS	Immune system
NES	Neuroendocrine system
NK-cells	Natural killer cells
NS	Nervous system
PE	Placebo effect
PNI	Psychoneuroimmunology
PS	Psyche
TNF	Tumour necrosis factor

Introduction

From the origin of life a struggle for surviving the natural environment has been going on. In addition all living beings have been competing each other in a biological battle for "the survival of the fittest"[1]. This competition exists between individuals of the same species as well as between individuals of different species. As for all wars, struggles and conflicts cause injuries in the participants and the development of strategies to protect itself from the injuring environments and/or aggressors.

One of the strategies humans developed to be on the winning site of the biological war is "medicine" or the art to protect for or cure diseases and injuries. In the past the chosen strategies and opinions in medicine have been under great influence of the dominating religion in a certain area. Whereas some ancient medical traditions still exist nowadays, others have developed further according to changing philosophies, technical progress and modern science. One striking question all these different medical endeavours bring about, is how such completely different medical methods and treatments sometimes can achieve the same healing effect. On the other hand, all over the world medical doctors, healers and medicine men/women who try to heal and cure human beings from their diseases, are confronted with the problem that what can make ill or cure one person, may be of no effect on another.

The interest which arises out of these observations is whether other mechanisms then those of a primary applied therapy are acting in the background and are influencing the healing process. One of these mechanisms might be the interaction between the immune,

[1] The catch phrase "Survival of the fittest" was first used by Herbert Spencer and tries to summarise the process that survival increases fitness only insofar as it increases later reproduction. The fittest individual, in the biological sense, is not necessarily the healthiest, strongest or fastest, but the one who is able to adapt to and survive the current environment. The modern meaning of fitness (strong, healthy, athletic etc.) needs not at all to be a supposition for higher reproduction rates. To be the "fittest" means to "fit in" the momentary environment and may include many features like fearfulness, weakness, social competence, emotional intelligence etc. also. These capacities can be as important for survival and reproductive success of an individual, as for a whole population of organisms, as well.

nervous system and the psyche. New insights in the functioning of these systems have shown that there is a close co-operation between all three and that this co-operation may be of importance in the process of healing. However, how this co-operation between the psyche and the neural- and immune system takes place and influences illness and healing is one of the most difficult questions to answer.

Aim of this project is to review the literature concerning this subject and, with the help of this literature review, (covering subjects like the history of medicine, psychoneuroimmunology, consciousness, body-mind) to postulate a theory on the regulatory and supporting mechanisms in the healing process.

Part one: a review of the literature

1 Health, illness and medicine; history, philosophy and culture
2 Psychoneuroimmunology
3 Body and mind
4 Mental states; emotions, moods, beliefs, hope and will
5 Placebo

Health and disease are two opposite conditions of living organisms, with a fluent vague crossing between the one condition and the other, as indicated by the definition of health used by the World Health Organisation: “health is a condition of complete biological, psychical and social wellness”. Disease starts with the insufficiency of the regulatory apparatus of an organism to keep or restore homeostasis (Virchow). On the one side of disease are the (biological) intruders, injuries or malfunctioning body cells, on the other side the function of the defensive regulatory apparatus. Medicine all over the world tries to support restoring homeostasis by destroying or eliminating the intruders or malfunctioning parts and / or supporting or enhancing the function of the defensive regulatory apparatus. Most of the modern scientific research is done on the elimination of the “intruder”, neglecting the factors involved on the side of the organisms own defensive apparatus. Whereas therapies and medication may differ from country to country and culture to culture, all medical doctors are dealing with the internal defensive systems. The aim of the following chapters is to give an overview of those elements involved and phenomena observed affecting the organisms own defensive regulatory system in the onset and recovery of diseases.

Chapter 1 describes the influence history, philosophy, different religions and cultures have on the attitude and view towards health and disease, resulting in those many different methods and therapies for cure, practised in the world. Thereafter, in chapter 2, aspects of the interaction between the organisms different internal systems involved and

regulating homeostasis and defence will be discussed. Whereas physiological body functions are well investigated and partially well understood the problem of “mind” influencing “psychological” as well as “biological” wellness is still a mystery. In chapter 3 theories on mind or consciousness will be described, and the consequences such theories may have on the physiological functioning of the body. Some important mental states suspected or believed to have influence on the onset and healing of diseases will be discussed in chapter 4. At last, the phenomenon of the placebo effect will be described in chapter 5.

1. Health, illness and medicine; history, philosophy and culture

1.1 The beginning

The art of healing is one of the oldest intellectual properties of human beings originated out of constraint, need, self-protection and the urge to help. The most primitive forms of medicine can be seen in the removal of and protection against parasites and invading objects, observed in animals as well as in humans. Feelings, similar to those experienced for invading observable foreign bodies, may have served as a basis for the primitive concept of “invisible foreign bodies” causing disease and first attempts to cure may have been similar to the removal of observable foreign bodies as findings on prehistoric sculls have shown.

The ability of humans to observe, learn and memorise increased their knowledge of the use of natural substances and methods supporting healing, and those most successful in applying these methods became medicine men or women. The development of consciousness, on the other side, increased the search for the meaning of life and death and initiated the establishment of religions. Because of the close relationship between life, death and disease, medicine and religion soon became closely connected and methods to cure mixed with religious rituals.

The first manuscripts pertaining to medicine descend from the ancient civilisations of Mesopotamia and Egypt (ca. 4000-2000 BC) and describe demon-magical medicine practised by priest-doctors as well as empirical rational acting practised by somatic doctors, basic element knowledge like fire, air, water, earth and the heart as central organ. Starting in the same time period Indian and Chinese medicine developed (2000-1000 BC). The Indian medicine was spiritually based, some elementary anatomies were known like blood, flesh, bone, fat and the wind-breath physiology. Growing within and beyond the boundaries of the mythic lore and epic battles of gods, conquerors and casts, Indian medicine developed in a series of distinct phases: a) prehistoric or pre-Vedic, b) Vedic and c) Ayurvedic. Medical knowledge was written down in the *Vedas* (the *Rigveda* from 4500-2000BC and the *Atharvaveda* 1500-1000 BC). Chinese medicine had a cosmic-biological concept with ancestor healing practises and demon-magical medicine, the development of the Yin-Yang doctrine, macrobiotics and pulse- and acupuncture teaching. In the following chapters the further development and basic philosophy of the global main stream medical practises will be described. The description will only discuss the most important and influencing events in the history of medicine and will be far from complete.

1.2 Western medicine

1.2.1 The ancient world

In contrast to the gradual evolution found in Egyptian, Indian and Chinese history, Greek civilisation seems to appear suddenly. Whatever their origin may be, the intellectual traditions established in ancient Greece provided the foundations of Western philosophy, science and empirical rational medicine.

➜ The Greek

Without more technological advances than other civilisations between 2000-0 BC, the Greeks managed to separate medicine from religion and placed disease on a far more rational basis than it had been ever before by mere extrapolation and rationalisation of the observed. The Greek were the first to note that diseases are natural. The most important person in early Greek medicine is Hippocrates who wrote some seventy books known as the *Hippocratic Corpus* . During the Greek era medicine became a science (at least for the physician) and the profession had to be underpinned with theory. The body was thought to consist of four principle humours - yellow bile, blood, phlegm, and black bile characterised by the same properties - dry, hot, wet and cold as the four elements - fire, air, water, and earth.

Table 1 **The four humours, elements and their characteristics according to Hippocrates**

Yellow Bile	**Blood**	**Phlegm**	**Black Bile**
Fire	**Air**	**Water**	**Earth**
dry hot	hot wet	wet cold	cold dry

One generalised theory was that disease was due to an imbalance of the fluid portions of the body. Hippocratic physicians studied anatomy, physiology and evident, immediate and obscure causes of disease.

In addition to the Hippocratic medicine many other smaller schools with cult or sect characteristic existed, some with complete opposite views and doctrines, like the anti-theoretical school of the empirical physicians of Alexandria, who mainly concentrated on the knowledge of pharmacological therapies and claiming that the study of anatomy was totally useless for understanding living beings.

➜ The Roman

The Roman Empire was a complex and vigorous combination of Greek and Roman cultural elements forged through centuries of war. Medicine had magic and folklore elements as well as empirical and rational elements. Aulus Cornelius Celsus wrote an encyclopedic work on medicine (ca 14-37 AD) and Pedanius Dioscorides one of the first herbals called the *Materia Medica.* According to Celsus the art of medicine could be divided into three parts: a) cure by diet or lifestyle, b) cure by medication, and c) cure by surgery. He rejected the Greek concept of the physician as necessary guide to health and considered it essential for every individual to acquire and understand the relationship between disease and the stage of life.

The most important medical school in the Roman era is represented by the work of Galen (129-199 AD). No other person in the history of medicine has influenced concepts of anatomy, physiology, therapeutics and philosophy as much as Galen. He expanded, commented and supplemented the *Hippocratic Corpus* with detailed formulations on the quality- and body fluids-pathology including their physiology. He increased his anatomical knowledge by animal dissections. The essential features of Galen's system were a view of nature as purposeful and the principle of balance among the four qualities and the four humours as already described by Hippocrates. Although Galen studied anatomy and physiology on an rational basis, he included spiritual elements as well, like in his pneuma theory (pneuma psychikon = soul pneuma (spiritus animalis) and pneuma zootikon = life pneuma (spiritus vitalis)). Whereas Hippocrates had Nature let heal, Galen was willing to interfere with the healing process. His most utilised therapy was bleeding, which he used for almost every disorder.

1.2.2 The Middle Age

During the following period no important new insights in medicine were developed. The Roman Empire became divided and most of the ancient medical texts were collected, summarised and newly categorised into compendia. Later cautiously own clinical experiences and, because of cultural exchange caused by the many different political and religious wars, Arabic, Persian and Indian medical knowledge were included.

➜ European Christian medicine

The birth of Jesus Christ and the following evolving Christian religion irrevocably transformed the status of the healing art. All Greco-Roman traditions based on intellectual curiosity, physical well being and glorification of the healthy body, were foreign to the medieval Christian world. Disease became a punishment for sin or a test of faith and being healed was not necessary good, however the quest for healing and health was never abandoned wholly by the laity and physicians and ways to justify healing were

defined by theologians. Medicine became divided into “heavenly” and “earthly” with own therapeutic methods. Whereas the “earthly” therapies included the use of for example herbs, the “heavenly” medicine used only words and prayers, as “Jesus had cured the sick by his word alone”. Christianity had a great, most intolerant and hostile, influence on the medical thought and science and attained a virtual monopoly. During the beginning of the Middle Age surgery became separated from medicine and was practised by oculists, bone setters and other empirics (barber-surgeons, herbalists, nurses, midwifes etc.). A new innovation during the Middle Age in Europe were hospitals, however they only provided comfort, nursing and care and the main goals were religious.

After 1130 however the monks were forbidden to practice and learn medicine and worldly medical schools were established such as the medical school of Salerno, Toledo and Montpellier. They deplored the separation of surgery and medicine, translated many Arabian texts into Latin, taught medicine and later became the first medical universities.

➜ Arabian Islamic medicine

The Middle Age of the European history roughly corresponds to the Golden Age of the Islam. Islamic medicine was as much influenced by the *Qur’an* as “Christian” medicine by the *Bible*, and fragments concerning medical lore culled from the *Qur’an* and the *Hadith* of the Prophet were gathered together as the “Medicine of the Prophet”. Although the Prophet generally recognised the natural causes of illness and the effects medical treatment had, disease was also connected with the supernatural and the disease was a way of God to test a person. In general the Islamic religion did not inhibit medical science, but all remedies in the end only worked by God’s will.

In the early period of the Arabian Middle Age many Greek and Roman medical texts were translated into Arabic (750-900 AD). Another significant achievement was the development of hospitals and hospital-based clinical training of medical practitioners, which were financially supported by the religious law of charitable endowments. Despite the honours accorded to scholar-physicians, scepticism about medical practise remained strong and Islamic traditionalists warned that the medical art was foreign to Arab culture.

One of the greatest, most scientific minded physicians of the Arabic world was Rhazes (ca 850-923 AD). He wrote the *Continens* (Comprehensive book of medicine), which was translated into Latin. To Rhazes the physician patient relation was of great importance, both having an ethical obligation, duty and trust to each other. He established the concept of specific disease (smallpox and measles) instead of defining them in terms of symptoms (fever, diarrhoea etc.). The first scholar to create a complete philosophical system in the Arabic language was Avicenna (980-1037 AD). He wrote the *Canon* for general practitioners and described the philosophical principles of medicine and the relationship

between the mind and the body, demonstrating how physiological phenomena could betray the hidden thoughts.

Although most of Arabian medicine comprised the preservation of ancient Greek wisdom, one important original contribution to medicine was done by the Arab Ibn an-Nafis (ca 1200 AD), who described the pulmonary circulation correctly.

1.2.3 Renaissance

The Renaissance period in Europe can be described as the age of the exploration of the word, the world, the mind, and the human body. The Greco-Roman-Islamic traditions were replaced by “modern” science, by the work of the medical humanists. Both artists (like Leonardo da Vinci 1452-1519) and physicians (like Andreas Vesalius 1514-1564) sought accurate anatomical knowledge and the human body became beautiful and worthy to study. During this period differences between the writings of Galen and own anatomical observations were made, but it was hard to reject the authority of Galen’s work. Whereas the anatomical knowledge increased greatly during the Renaissance, physiology stayed on the level of Galen.

The renaissance was not only a period of rational medical science but also an age of superstition and occult science and medicine remained entangled with astrology, alchemy and mysticism. Astrology incorporated the motions of the heavenly bodies in diagnosis and therapy and alchemist tried to develop drugs and thought that the vital functions of the body depended on a mysterious force called the archaeus (internal alchemist). In opposition to the concept of humoral pathology and the doctrine of Galen, the alchemist Paracelsus attempted to substitute the doctrine by the principle that the body was essentially a chemical laboratory. Disease was, therefore, the result of derangements in the chemical functions of the body and should be cured by specific chemical substances.

1.2.4 Revolution (seventeenth century)

During the sixteenth and seventeenth centuries a great transformation of the physical sciences occurred by the work of Copernicus, Galilei and Newton. Revolutions in medical science were given by William Harvey, who discovered the minor and major blood- heart-lung- circulation, or Antony van Leeuwenhoek, who invented the microscope. The increased insight in nature and physics demanded for new theories in medicine. Two main stream health and disease concepts developed namely:

1. Paracelsic Iatrochemy

Following the ideas of Paracelsus the body fluid doctrines of the ancient medicine were rejected and all body functions were seen as chemical processes. Although this chemical

doctrine was not able to explain all the natural occurring phenomena and still was much influenced by spirituality and religion, it became an important component of modern (now a days) medicine.

2. Iatrophysic, iatromechanics and iatromathematics

Whereas iatrochemy still was preoccupied by the body fluids, iatrophysical health and disease concepts totally turned away from humoral-pathological thoughts, and tried to implement the new insights of physics into the living. The most important representative of iatrophysic is René Descartes (1596-1650), who reduced all body functions to physical-mechanical principles. The only exception he made was for the Glandula pinealis which was thought to be the central organ of the thinking soul.

Although many new theories developed, for daily medicine they had not many impacts on the cure and treatment of diseases.

1.2.5 The age of Enlightenment

During the past period, thinking and handling was strongly dominated by doctrines and religion. This changed during the eighteenths century where thinking and reason became independent from the church and state. The scientific leitmotiv changed to empirism and rationalism, with systematic observations and planned experiments. Different old health and disease concepts were renewed or replaced by new ones.

Many theories were postulated which can be divided in two categories: the physical/mechanical theories and the spiritual theories as listed in Table 2. All these different theories initiated the separation between a material body orientated medicine and a soul/mind orientated medicine.

The eighteenth century is also the age of the founding of the modern hospital with inner medicine, surgery and pharmacology.

Table 2 Overview of health and disease theories in the eighteenths century

Physical/mechanical theories	**Spiritual life force theories**
Bio-mechanics of Friedrich Hoffmann (1660-1742) All body states in health and disease are dependent on the tonus of the fibre parts of the body, in particular those of the fluid transporting system. The living is created by God, who rules over all mechanical processes.	**Psycho-dynamics or animistic** theory of Georg Stahl (1660-1734) The causing principle of health and disease is the feeling, perceiving, willing and acting soul. All body systems get their energy from the soul, the soul rules and the body serves the soul.
Mesmerism of Franz Anton Mesmer (1734-	**Vitalism**

1815) Every organism has a magnetical fluid which can be influenced	The animistic theory was further developed by some French physicians, who postulated a “Principle of Life” responsible and causing all living. The “Principle of Life” was in charge of fundamental and acting forces and disease was seen as disturbance of the “Principle of Life”.
Irritability or sensibility of Glisson (1597-1677) and Haller (1708-1777) Provocative nature of the muscles determines perception	**Life force theory** of Chr.W.Hufeland (1762-1836) Life force as life preserving principle of the organism is closely related to natural healing forces.
Brownianism of J.Brown (1735-1788) The stimulating impuls is life promoting. Internal and external stimuli excite and uphold life. Health and disease are determined by the irritability of an organism.	

1.2.6 The nineteenth century

The nineteenth century is the century of the industrial revolution and early capitalism. It is also the century of the origin of modern empirical-experimental science and medicine, the development of pharmacology, cell pathology and bacteriology (Pasteur). New instruments allowed new scientific investigations, diagnosis and a rationalisation of therapies. During this period the physical and psychical body were further separated and medicine became more and more the science of the material body. With the evolving knowledge of the different body organs, physicians started to specialise in different disciplines according to the corresponding body organs or functions. Medical treatment became available to almost the whole population and medical health and accident insurance institutions were established.

The successes booked in physic and chemistry more and more influenced and determined the medical science, methods and therapies, however did not hinder the appearance of different theoretical schools such as :

- The natural philosophical physiology with the vegetative (growth, nourishment and reproductive forces), animistic (irritability of the organs and muscles) and sensitive (sensory, nerves and soul) dimension.
- The natural scientific physiology which was completely based on the scientific investigation of body functions.
- The cell-pathological theory of Virchow (1821-1902), who declared that all diseases resulted out of changes in the cells, and that the cell was the true organic unity of the

body and the part of departure for all life. His theories were transmitted to society and resulted in the development of bio-socialism.

The development of bacteriology by Louis Pasteur (1822-1885) and Robert Koch (1843-1910) for the first time proved the ill making potency of micro-organisms which initiated the science of microbiology, modern vaccination and the development of disinfecting agents to be used during surgery.

Not all physicians accepted the scientific developments in medicine and out of vitalistic and life force theories of the eighteenth century alternatives arose like the homeopathy of F.S.Hahnemann (1755-1843). According to Hahnemann disease is an affection of the life force by pathogenic disturbers and has to be seen as a holistic body phenomenon. Instead of supporting the body's resistance, a homeopathic physician applies low or lowest doses of substances which evoke the same symptoms as caused by the disease itself. The so provoked artificial disease stimulates the life force to increased resistance.

In addition to homeopathy naturopathy developed with hydrotherapy to support the natural discharge of

The separation between body and psychic illness proceeded during this century and the brain became more and more the object of investigation for psychic illness and abnormalities (pathological- and somatic psychiatry). As for body medicine, alternatives to the scientific views were established like the psychoanalysis of S.Freud (1856-1939).

1.2.7 The twentieth century

The last 90-100 years have been years of immense technical improvement in medicine. Newly developed diagnostic (X-ray, nuclear spin resonance, biochemistry, genetic and molecular methods) as well as therapeutic (antibiotics, chemo- and radiation therapy, micro-surgery, gene manipulation, etc.) methods have brought great advancements and possibilities to cure diseases untreatable up till then. In addition the work of the early alchemists evolves in modern pharmacology and the research and production of medication is industrialised and commercialised. Medicine and pharmacology become political issues, for example the development of eugenics during the first and second worldwar, as well as commercial issues such as healthcare insurance companies. Medical research is no longer determined by exclusively and pure curiosity but is controlled by ethical as well as financial and commercial elements.

One of the highlights in medical science is the discovery of desoxyribonucleic acid (DNA) by G.Watson (1928-) and H.Crick (1916-) and the gene as information carrier of all biochemical substances of the organism. Many diseases now become reduced to gene mutations. The discovery of DNA on the one side reinforces the materialisation of

medicine, on the other side leads to the development of Darwinian medicine (the egoistic gene, why do mutated genes survive?).

Because of the enormous technical progress in medicine, the life expectancy increases rapidly, however many people lose their belief in the technical materialistic medicine as they threaten to become a “body without a soul” in a factory called healthcare or hospital. When even the advanced techniques may fail to cure and the side effects of a therapy are worse then the disease itself, alternatives are searched for in old traditional medicine such as Indian or Chinese medicine, as well as in new (for example anthroposophic), partially sect like (for example esoteric-, spiritual-, aura healers etc.), gentle healing methods. These medical methods find even more confirmation when it becomes clear that many disease causing micro-organisms and viruses mutate and become resistant to medication (like antibiotics) faster than new medication can be designed against them.

In spite of the fact that modern medicine has improved health in western cultures to a standard never seen elsewhere on earth, its achievements stay below it’s promises. The loss of confidence in modern medicine seems to take place parallel to the loss of confidence in the authority of the Christian church in western countries and stimulates the search for a new sense of life, including a new sense of health and disease. One of the newest interests is the role of the brain in consciousness, mind and soul, and the influence these non- (?) material elements can have on health and disease. In addition to technical biomedicine the call for more holistic, body and soul integrating medicine becomes loud.

1.3 Asian medicine

In contrast to western medicine the constant shifts in ways of thinking about health and disease seen in western cultures, did not occur in such extent in Asian cultures. Instead of the evolving interest in anatomy, molecular and biochemical reductionism of body functions and separation of body and mind by the western physicians and medical researchers, Asian medicine in general holds up to the humoral concepts of body functions. Physiological, pathogenic or therapeutic processes are explained in terms of perceptible qualities of the ubiquitous humoral fluids, expressed in contrasting pairs hot/cold, dry/wet, active/passive, light/dark etc. These qualities are applied to body components as well as to mental states, environment and climate, integrating man with a spacio-temporal universe. Body and mind are seen as interdependent poles of the same somatic and psychic continuum, interrelated with the world and society.

1.3.1 Indian *Ayurvedic* medicine

The classical system of Indian medicine is called “the knowledge for longevity”, or in Sanskrit *ãurveda*. The theoretical doctrine is based on the three body humours wind, bile and phlegm and its therapies are herbal, massage, ointments, enemas, douches or surgery.

The earliest surviving textbooks of *Ayurveda* , written in Sanskrit, date from the first centuries AD. The two most important texts are the *Caraka Samhitã* and the *Susruta Samhitã*, which form the cornerstone of *Ayurveda.* Both texts emanate from a single medical tradition and contain philosophical passages as well as descriptions of sophisticated surgery. Later new important texts are implemented like the *Astângahrdaya Samhitã* (700 AD) or the *Sãrngadhara Samhitã* (1400 AD).

The basic theories of Ayurvedic medicine are related to the *Sãnkhya* philosophy, which postulates that there is no universe before creation occurs, and all that exists is “pure reality”. The cosmos and “pure reality” cannot be separated because “pure reality” is cause and cosmos is effect. For body and mind this means that body evolves from mind, but mind is dependent on body.

The body is thought to consist of the same five elements the universe is made up of: earth (hardness), water (moisture), fire (heat), air (vital breath) and space (the interstices and the self by indwelling spirit). Combinations of the five elements condense into the three *dosas* : *vãte* (air and space) *pitta* (fire and water) and *kapha* (water and earth). A *dosa* is any fault or error, any transgression against the rhythm of life which promotes chaos. The different *dosas* are in charge of different functions in the body : *vãte* for all motion in the body and mind, *pitta* for all transformation and *kapha* is the stabilising factor. Life is inconceivable without these three activities and any imbalance causes disease.

From the *Ayurvedic* perspective one should take care of the body, for in the absence of the body there is the total extinction of all that characterises embodied beings. Diseases, which can affect mind and/or body, are divided into two types: those which arise from within, and those arising from without. Both mental and bodily diseases can be transformed into and expressed by each other and intensive (negative) emotions are assumed to be of great influence on the onset of disease.

Ayurveda’s diagnosis concentrates on the relationships between the body and mind of the individual in the “now” and the direction one is changing to. From the side of the physician curative energy towards the patient is demanded for since reinforcement of faith and hope during the diagnostic process can initiate the healing process. The applied therapy first has to be rightly timed and is essentially of two kinds: purification and palliation. Palliative drugs should protect the tissues they enter, from the attack of the *dosas.*

Although India has been occupied by the British, which suppressed *Ayurvedic* practises and introduced western medicine, after liberation *Ayurvedic* medicine has regained an important part of the Indian healthcare system with own universities and journals.

1.3.2 Indian *Unani* medicine

Unani medicine is practised by the Islamitic population of India, has its roots in the schools of Hippocrates and Galen and is closely related in its development to Islamic medicine in general. In addition to the three humours (phlegm, bile and wind) of *Ayurvedic* medicine, *Unani* medicine recognises the forth humour blood. Other similar elements in both medical systems are their view on the necessity of humoral balance and the holistic approach to health. Both systems have learned and use methods from each other which has influenced their further development.

The theory of *Unani* pharmacology is based on the ideas of Galen. Drugs have the same temperaments as humans (hot, cold, wet ,dry) and are graded into four degrees of potency. Because drugs described by the Islamic medical textbooks were not always available in India they had to be replaced by other drugs with the same degree of strength. In addition *Unani* physicians steadily increased their knowledge by borrowing from *Ayurvedic* sources. Today *Unani* medicine has remained a vibrant tradition which provides relief for a large number of Indian populations.

1.3.3 Tibetan medicine

Tibetan medicine appeared later in history than the other Asian medical tradition and the first Tibetan medical texts date from the fourteenth century. The medical tradition is closely tied to with Buddhism and influenced by Indian and Chinese medical traditions. With the Fifth Dalai Lama (1642) a new era for Tibetan medicine began, as he promoted the teaching and science of healing and re-editing of the *Four Tantras*, the fundamental reference work of Tibetan medicine.

The theory of Tibetan medicine shares the same background of the five elements space, wind, fire, water and earth and their qualities hot, cold, dry and wet with the other Asian cultures. The five elements are perceived by the five senses and their combination, in variable proportions, results in the infinite multitude of substances which are characterised by certain perceptible qualities (hot/cold, heavy/light etc.).

The body is a complex and varied aggregate of the five elements and sentient beings have no reality of their own but are the temporary conjunction of the five phenomena form, feeling, perception, volition and consciousness. The mind or consciousness transmigrates from one existence to another when the aggregates which make up the apparent

personality disintegrate at death. According to the Tibetan culture life, health and illness involve the constant dynamic interaction of all these elements. Since Buddhism is the religion of the rebirth of the mind, the body is only a temporal seat of the mind. On the one side the body is an instrument to enhance spiritual advancement and therefore has to be kept in good condition, on the other hand the body is no object of attachment.

Tibetan medicine borrowed most of its theories concerning physiology, pathology, diagnosis and therapeutics from Indian *Ayurvedic* medicine (the three humoral fluids with their characteristics, the seven body tissues which are produced by digestion and their residues generated by their metabolism). Disease is not seen as a foreign entity which contaminates the body from the outside, but rather as potentially inherent in the very nature of the vital principles themselves. The three humours are the physiological agents responsible for health as well as for illness. The humours may become pathogenic under the influence of season, environment, conduct, diet, poison, trauma and evil spirits. Psychosomatic triggers of illness are seen in the three poisons desire, anger and ignorance which can create imbalance in one of the three humours.

Diagnosis has to be compassionate and is achieved through three channels of investigation namely, touch (of which the most important is the palpation of the pulse), visual (urinalysis, tongue) and questioning.

The treatment of Tibetan medicine is based on four types of “antagonists” : humours in excess are usually treated with opposing qualities applied by 1) conduct (behaviour), 2) diet, 3) medicine and 4) external therapy (mild like compresses, or drastic like blood-letting). Therapeutic substances are applied according to their taste qualities (taste affects humours) and their potencies, which form pairs of opposites (cold/hot etc.). Most Tibetan medical preparations combine various ingredients according to an understanding that the effects of the main drug must be tempered, corrected and orientated by the action of the secondary ingredients.

Although Tibet has suffered the occupation by the Chinese communists, and big parts of its culture and medicine have been destroyed, recently Tibetan medicine has become accepted by the governing Chinese authorities through its sheer efficacy and cheap treatments.

1.3.4 Chinese medicine

The traditional Chinese medical theories are based on the *Taoist* concept of body functions and its ideas about the internal world of the human body. The body is viewed as a small world, country or model of the universe, who’s landscape is governed by a ruler and its assisting officials and ministers. Only the harmony and the co-operation between

the members of the government results in health and achieved by transport and communication. In addition the body is inhabited by spirits, which live in the body's important areas and take care of its different functions. In and outside the body there is a "moving thing" called *qi* which has its natural direction and rhythm, is omnipresent and when acted contrary to, is liable to contract diseases because it has become blocked somewhere in its circulation. *Qi* is the representation of movement and change, which are essential to Chinese philosophy. Change is created by the interplay of two forces, *yin* and *yang.*

The basic cause of disease according to *Taoist* medicine is the lack of "rest" and so the mind should remain quiet, which can be achieved by exercises. Disease and its cure are understood in the *yin-yang* terminology and can be caused by external and internal factors. Diagnosis is based on the four elements 1) looking, 2) listening, smelling and tasting, 3) interrogation and 4) touching, and therapy on the *yin-yang* principle that the opposite of what is causing the disease will cure (cold versus heat, but heat versus heat when heat is caused by cold like fever is caused by a cold). There are eight methods of therapy that form the basis of any technique of therapy (acupuncture, massage, drugs etc.) namely sweating, vomiting, lowering, harmonising, warming, purifying, dispelling and supplying. The best known Chines therapeutic technique is acupuncture, which is a way of influencing body functions by inserting needles in the *xue* or acupuncture points. Acupuncture is often combined with moxibustion or burning of the herb moxa placed on the body. Another therapeutic technique is massage of which different systems exist. Chinese pharmacology uses herbal, mineral and animal components according to their medical nature (cold, hot, etc.) and taste. Only when these above mentioned therapeutic techniques fail the traditional Chinese physician will use surgery.

Chinese medicine is much more diverse than the other Asian medical traditions and sharing of traditions, theories and therapies, for medicine as well as for religion, is common to the Chines people. The mix of traditional Chines and Western therapies used nowadays by Chinese physicians, is completely accepted, however creates paradoxical ways of explaining and curing diseases and is more disconnected from the roots.

1.4 Other cultures

Other cultures with an ancient history of medicine are the Aztecs of Mexico, the Maya culture of Yucatan and the Inca culture of Peru. All medical knowledge in these cultures was property of the priests and therefore strongly influenced by religion and astrology. None of these medical cultures has left behind medical textbooks such as those of the Western and Asian traditions and although remainders of the tradition still may be

practised by folk physicians today, they did not grow out to a “world” medicine. The same must be said for medical traditions of for example Africa or Australia. Because of the occupation and colonisation of big parts of these worlds by Western cultures and the strong missionary compulsion of the Christian religion, medical traditions of the native population were partially or, when forbidden, completely replaced by Western medicine. Today still existing medicine of primitive cultures is furthermore under great religious and spiritual influences and of great importance for the study of the development of medicine and medical thinking.

1.5 Summary and comment

The history of medicine is a history of beliefs, rituals and rational thinking and may be separated into two main streams, namely a medicine based on (religious) beliefs and an influential mind, and a medicine based on mindless rational materialism, whereas the latter appears later in history and is mixed as well as in conflict with belief/mind based medicine. The element both streams have in common are rituals. Whether a healing dance, the setting of acupuncture needles or a CT scan, all evoke mystic feelings as their mechanism of action in general is/may not be understood by a patient.

One of the ostentatious characteristics of on rationality based (modern) medicine is its inconstancy. Treatments thought to be advantageous at one time may become out of use less then 10 years later and are replaced by new more advanced therapies, which themselves may be replaced some time later. The tremendous amount of medical and pharmacological research brings physicians in a position of choice: not one but many treatments may be possible of which the effectiveness of all of these treatments may not be for sure. Modern biomedicine, although with a high standard, is a medicine of uncertainties. One of the reasons may be that in those societies where matter rules over mind and beliefs and religion have lost a public state and are extruded to privacy, biomedicine is losing confidence because it lacks a “belief and/or mind factor”. A society or science may have left beliefs and religion behind, patients haven’t and the more scientific medicine gets, the more it detaches itself from the needs of those who rely on it. In those societies which have long relied on rational material medicine the appearance of all kinds of ancient and new alternatives, some with funded knowledge and proved effectiveness, others with obscure unproved mechanisms of action and effectiveness, but all implying some sort of belief, religious and/or mind based background and “rituals”, indicate the individual’s need for a “belief/mind factor” in medicine.

In contrast, medicine based on ancient beliefs/mind traditions is a much more constant medicine. Even though this type of medicine may adapt modern knowledge, its basic

principal is not changed and treatments rely on constancy. A “belief/mind factor” is actively implemented in the treatment and no need for change and renewal seems necessary. The mechanisms of action of treatments may not be determined or proven according to modern scientific criteria, however excluding a “belief/mind factor” in investigating a mechanism of action may lead to these conclusion.

Because all kind of treatments seem to have at least some sort of success, and no medical strategy is able to cure all illnesses it can be asked whether a basic conformity exists between the applied healing strategies or whether ill individuals may be able to evoke a basic healing mechanism. In addition what most people on earth seem to have in common is their ability to stay healthy most of the time. Maybe future medical science will show the mechanism involved in staying healthy, which in turn can help to understand the mechanisms involved in healing. The following chapters describe some of the factors involved within an individual supporting health and healing.

1.6 Literature

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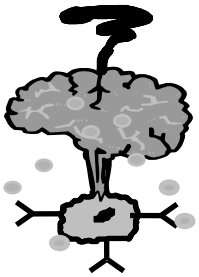

2. Psychoneuroimmunology

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2.1 Introduction

Psychoneuroimmunology is a rather new science which tries to understand the interactions between the immune system, being the defence apparatus against ill making intruders or malfunctioning cells of an organism, the nervous system, controlling all body functions, and the (more difficult to define) psyche (PS).

As early as the beginning of this century different investigators started to observe interactions between molecules of the nervous system (NS) and the immune system (IS). However these investigations were soon forgotten and research focused on the effects of stress on endocrine variables. Only many years later G.F.Solomon published a paper entitled “Emotions, immunity, and disease”. In this paper the term “Psychoneuroimmunology” (PNI) was used the first time. Another 20 years later Ader&Cohen summarised an impressive amount of data showing the functional interaction between the NS, IS and neuroendocrine system (NES). Although one domain of the PNI research focused mainly on the “material” side of the interactions between IS, NS and NES, a second direction started to investigate the psychosocial components influencing immunity and its effects on health and disease. A third direction investigated the influence of immunity on psychological disorders and behaviour. Data concerning these last two fields of investigation are often more difficult to interpret and are sometimes controversial as psychological elements can be less well defined and measured. Still, PNI research offers an opportunity to integrate a mindless body medicine with a bodiless mind medicine and might offer answers on the heterogeneous reactions of humans on obvious similar situations in health and disease.

In the following chapters models on the hierarchy and architecture of interaction between PS, NS, NES, and IS will be postulated, and the belonging interaction and communication pathways discussed in detail.

2.2 PNI interaction models

Before discussing detail interaction pathways between PS, NS, NES and IS it is important to first think over the general hierarchy and architecture of the involved systems. Different models of hierarchy influence the art of how research on the interaction mechanisms was/is planned and can influence the interpretation of the collected results. Which of the models is “true” can hardly be answered as it depends strongly on the opinion a researcher has on the Body/Mind interaction topic and all the below listed models therefore may be as true as they can be false.

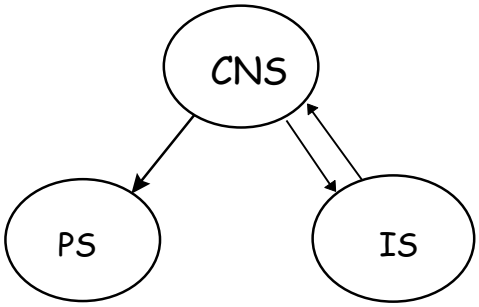
The used terms in the diagrams have the following meaning:

CNS - Central nervous system including the brain, neurotransmitters and the neuroendocrine system.

IS -Immune system including all immune organs, cell types and their soluble products.

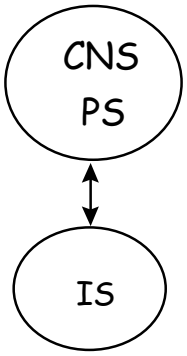
PS - Mind, soul (un)consciousness, thinking, feelings, emotions, behaviour, personality.

Figure 2–1 **The CNS as boss**



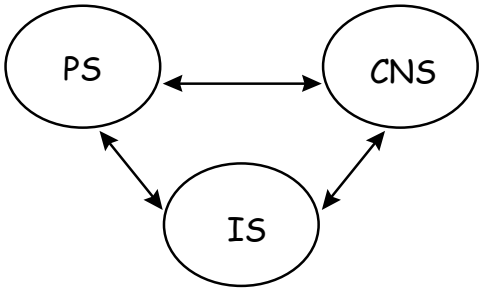
The first model which considers the CNS on top of the hierarchy. The PS is a product of the CNS and the IS is considered to be the sixth sense supplying the CNS with information on the health state of the body. However, only the CNS has control. The CNS has influence on the PS and the IS, but not the other way around.

Figure 2–2 **CNS and PS are one and the same**



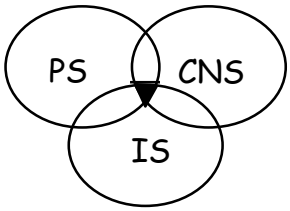
In the second model the CNS and the PS are one and the same. As such they have influence on the IS. The IS can modulate CNS activity which may have an effect on the PS. The CNS/PS complex however is superior over the IS.

Figure 2–3 **PS, CNS and IS as (equal) separate systems**



In this third model the CNS, PS and IS are three separate systems. They are all connected with each other with own communication factors which can be understood by the others. All systems have a more or less degree of autonomy but changes in one system can have direct or indirect influence on the functioning of the other systems.

Figure 2–4 **Integration**



The last model tries to integrate the three systems. Communication and interaction can take place by shared factors. The functioning of the systems depends, at least partially, on each other.

Only part of the communication factors between the three systems are known by now and a complete picture and model of how PS, CNS and IS are related and what the biological functions of these connections are, is not cleared in detail yet. In the following the known connections and their biological functions will be discussed.

2.3 Neuro - immunology

The connections between the CNS and IS are the best investigated aspects of PNI up till now and cover nerve fibers innervation of lymphoid organs, the neuroendocrine system and cytokines. Most of the investigations focused on the stress induced neural- and neuroendocrine alterations and their effects on the immune response. Although the biological relevance of these connections are not all cleared, the results show that the IS is not an autonomic organ and that the co-operation with the NS is immensely complex.

2.3.1 From the central nervous system to the immune system

➜ Nerves

The connection from the CNS to the IS involves several pathways. The most direct way is that primary (thymus, bone marrow) and secondary (e.g. spleen) lymphoid organs are innervated by noradrenergic nerve.The contact between lymphocytes and nerve endings is synaptic-like. In addition, T- and B- lymphocytes, neutrophils, mononuclear cells and NK-cells posse α- and β-adrenoceptors. The function and modulatory effects of noradrenergic innervation on immune functions may differ depending on the types of cells and receptors expressed on the cell surface of these cells and can inhibit as well as stimulate certain immune.

➜ Neuroendocrine

The second indirect way the CNS can communicate with the IS is through the NES. Releasing factors from the CNS cause endocrine glands to secrete hormones into the circulation. A good example are the hormones produced by stress. Physical and/or psychological stressors lead cells in the paraventricular nucleus of the hypothalamus to synthesize and release corticotrophin releasing hormone (CRH) into the portal blood system of the brain. In the anterior lobe of the pituitary gland CRH stimulates the synthesis and release of adrenocorticotropic hormone (ACTH) into the peripheral blood. ACTH ultimately causes the release of glucocorticoids from the adrenal gland. Most leukocytes exhibit receptors for glucocorticoids and are inhibited in their function by these hormones.

One function of immune suppression by stress hormones can be seen in the reduction of energy consumption in those on going processes which are not primarily necessary for the elimination of the stress. Another function of immune suppression by glucocorticoids is the inhibition of non-specific immune responses to antigens.

Many other neuroendocrine components have *in vivo* immune-modulating capacities and are listed in Table 3. Furthermore receptors for other neuroendocrine factors (ACTH, neuropeptide-Y, follicle stimulating hormone, luteinizing hormone) have been found and some of these hormones have *in vitro* effects on the activity of certain leukocytes.

Table 3 **Overview of neuroendocrine substances with *in vivo* immune-modulating capacities**

HORMONE	Function	Receptor on Immune cells	Effect on immune function
Catecholamines Adrenaline/ Noradrenaline	important for fight or flight reaction stress hormones	β_2-Adrenoceptors on all cells	↓ T-cell reactivity ↑ NK-cell activity and migration
CRH	start signal for the hypothalamus-hypophysis-adrenal gland axis	spleen macrophages	indirect ↓ of NK-cells
β-Endorphin	opioid peptide with morphine like functions	all cells	↑(↓) T- cell reactivity and NK-cell activity
Enkephalin	endogenous opioid	Leukocytes and lymphocytes	↑ NK-cell activity
Glucocorticoids	↑ Glucose production in the liver, effects on metabolism	All immune competent cells	↓ cytokine production ↓ T-,B-cell reactivity and NK-cell activity general immune suppressive
Growth hormone	important for normal growth and development	T-lymphocytes, mononuclear leukocytes	↑ T-cell reactivity and NK-cell activity increases thymus size
Prolactin	physiological function unclear	T-,B-lymphocytes, NK-cells (?)	↑ T-, B-cell reactivity
Substance P	↑ Intestine activity, ↓ Blood pressure, microvascular permeability	T-,B-lymphocytes	↑ Antibody production, ↑ Lymphocyte proliferation
Thyrotrophin	basic metabolism	Phagocytes, B-lymphocytes	↑ Antibody production

↑= stimulating, ↓= inhibiting,

➜ Nerve cell derived cytokines

A third communication pathway between the NS and IS might exist in nerve cell derived cytokines. Gliacytes and astrocytes have been found to secrete cytokines like Interleukin-1 and 6. Interleukin-1 (IL-1) may serve as a neurotransmitter in the brain.

2.3.2 From the immune system to the central nervous system

➜ Cytokines

During an on-going immune response induced by intruders like viruses or bacteria many different soluble products are produced by leukocytes which, in the first place, are necessary for a normal functioning of the immune response. These products are:

- Antibodies
- Interleukins
- Interferones

- Tumour necrosis factor (TNF)

The functions of these soluble products are manifold and in general can be described as regulatory (differentiation, multiplication), stimulating and/or inhibiting certain functions and activities of the different cells of the IS. Beside, these products have direct or indirect (via the NES) influence on the CNS.

Direct: cytokines seem to be able to change the firing frequencies of nerve cells in the CNS and influence the secretion of neuroendocrine factors involved in the hypothalamus-hypophysis-adrenal gland axis, especially the production of ACTH. Receptors for cytokines like IL-1 have been found in the CNS and pituitary.

How a big molecule like IL-1 is able to cross the brain blood barrier is still a question under investigation, but this barrier is not present in the area of the pre-optic nucleus of the hypothalamus and neurones in this area express receptors for IL-1, TNF or IL-6. Indirect: cytokines like IL-1 have influence on the secretion of prolactin, sex-, thyroid stimulating-, and growth hormone.

The biological function of these interactions are in the first place to establish a feedback loop between the CNS, NES and IS for the regulation of the on-going immune response. Secondary the cytokines might function as the sensory input for the CNS for non-cognitive stimuli like viruses, bacteria, antigens or cancer cells What can't be seen, smelled, heard or felt is recognised by the IS and reported to the CNS by cytokines.

➜ Immune cell derived neuropeptides

Like nerve cell derived cytokines, immune cells are able to produce neuropeptides. T- and B-cell mitogens like phytoheamaglutinin, Concanavalin A or Candida albicans can stimulate these cells to produce ACTH and β-endorphin Other hormones or neuropeptides which can be produced by activated immune cells are TSH, growth hormone, enkephalines, CRH and substance P.

The production of endorphins and encephalines by activated immune cells may induce an analgesic effect in the infected tissue. The function of the other produced hormones and neuropeptides can inhibit or stimulate inflammation or may influence/induce behavioural changes.

2.4 Psycho - immunology

Six hundred years AD, in a famous compilation of texts, covering the theories of classical Indian Ayurvedic medicine, called *Astangahradaya Sustrasthana,* , it is written that " The physician should reject that patient…..,who is busy with other activities; …who is violent, afflicted with great grief, full of fear…. [*Astangahradaya Sustrasthana* 1/34-35a in . 1 page 96]. Poor prognosis is given to patients who are afflicted by intensely negative emotions because hatred, violence, grief, ingratitude and other derivatives of *raga* (desire, passion) are so much stronger than the body's capability for homeostasis. When the patient is unwilling or unable to abandon this passion they will create new diseases just as fast as the doctor can remove the old ones.

Even though a relation between the mental state and disease has been observed and described already so long ago, modern biomedicine has long refused to see any connection. Although mental states are difficult to characterise and define by means of pure materialistic science, PNI tries to investigate the observed empirical findings.

Psycho-immunology addresses to the role of psychological factors in physical illness, as well as the role of the IS in behavioural changes and it's possible connexion to mental illness. Some of the connections between the PS and the IS are described in terms of molecular-, hormonal- or neuropeptide interactions (for example the stress reaction or sickness behaviour). Other mental states are neurophysiologically less well defined and their influence on the IS might be by indirect behavioural changes. In addition alterations in the immune function have been postulated to be responsible for psychological disorder like schizophrenia.

In the following chapters some of the investigated relations between the PS and the IS will be listed. However, because of the manifold psychological, psychosocial and personality variables, this list of interactions will be far from complete.

2.4.1 From the psyche to the immune system

The influence psychological factors have on the IS are in the first place dependent on internal innate (genetically) dispositions and the influence these dispositions have on primary behaviour. Secondary, internal dispositions will influence the behavioural output after external stimulation. This means that the internal effects on external psychological factors may vary greatly from one person to another. Psychological influences on immune functions therefore should be regarded, on the one side, in context of internal personal

factors and on the other side on the effect external psychological stimuli in general have on an organism.

➜ Internal: Personality and the immune system

The role of personality in health has been a subject of great interest for many years although its relation to immunity has received little attention. Investigations concerning immune status and personality characteristics involved in coping strategies have shown that immune suppression, stimulation, or no influence can be found. Different methods used for scoring personality characteristics might be one of the most important sources of contradiction. Besides, the reduction to only one personality characteristic or coping strategy, for examining the effect of personality on the IS, expels the influence different personality characteristics have on each other. Still, by their influence on the immune status personality dispositions may be responsible for the susceptibility to certain diseases.

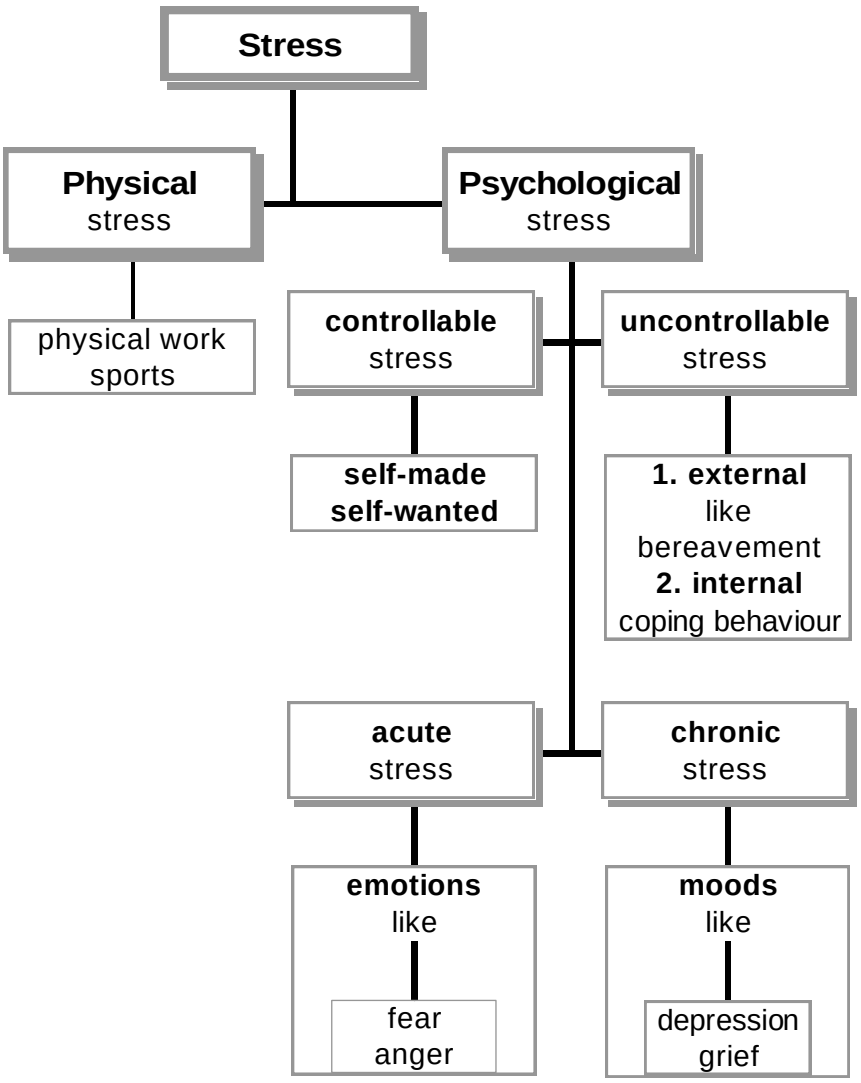
➜ External psychological factors: Stress

Stress is one of the most frequent mentioned psychological factors in relation to the IS. Thereby is stress one of the least well defined psychological factor and controversies, in the found results concerning immune modulation, are manifold. Figure 2–5 tries to characterise different possible stress types, which in reality mostly occur in combination, for example (un)controllable emotional stress or (un)controlled physical stress. Whether all stress induced immune modulatory effects are based on the same physiological mechanism or are caused by different mechanisms is still under investigation. A good review of stress and the IS is given in the textbook of PNI by Schedlowsky and Tewes.

- acute controlled emotional or mental stress

For this type of stress, experiments like parachute jumping or mental tasks (for example the “Stroop-Colour-Word-Conflict” test) were used. Increased numbers and activation of circulating leukocytes, in particular NK-cells, were found. The rather short lasting stress related immune modulation in these situations is associated to increased catecholamine levels (see Table 3, page 32). Although catecholamines act immune suppressive *in vitro, in vivo* they seem to call the IS on “stand-by”. Catecholamines belong to the “fight or flight” reaction and in past times the IS had to be “stand-by” in case of injury. Nowadays this function may have lost its significance in most cases but still is a “normal” physiological reaction and in general, does not have consequences for health.

Figure 2–5 **Different kinds of stress**



- Chronic uncontrollable negative stress

Chronic uncontrollable negative stress like bereavement or academic examinations, in contrary can cause suppression in activity of several immunological parameters. Part of this suppression may be due to the activation of the neuroendocrine CHR-ACTH-glucocorticoid pathway. Moreover lack of appetite or insomnia can have indirect influences on the IS. In addition, the psychosocial environment seems to play an important role. Because no norm values for most of these immunological parameters are available or defined, it is hard to say when a digress from the “mean” becomes pathologic

- Chronic controlled stress

Chronic positively experienced controlled emotional or mental stress, like an intensive period of hard but interesting work, seems to increase physical wellness and immune function, which may collapse as soon as the stressful situation has past by. Part of this immunological “high” may be due to elevated levels of endorphins and enkephalines.

- Depression

Correlations between depression and elevated susceptibility for infections or mortality rates have been observed and are associated with immune suppression. In spite of extensive research, up till now no uniform outcome could be established. Heterogeneity of depressive disorders can be made responsible for these discrepancies, but also different coping behaviours, sleep habits, food consumption and/or psychosocial environment. Although elevated ACTH or glucocorticoid levels seem to be responsible for some of the found immune suppression, not all immune suppression can be correlated to changed neuropeptide levels as in many cases no elevation of these peptides could be found. Although depressive disorders can be brought in context with elevated infection rates, but not severity of the infection, no clear relation to the increased occurrence of cancer could be confirmed. However, psychological or psychiatric interventions in cancer patients have shown to be able to reduce stress and increase immunological functions and survival.

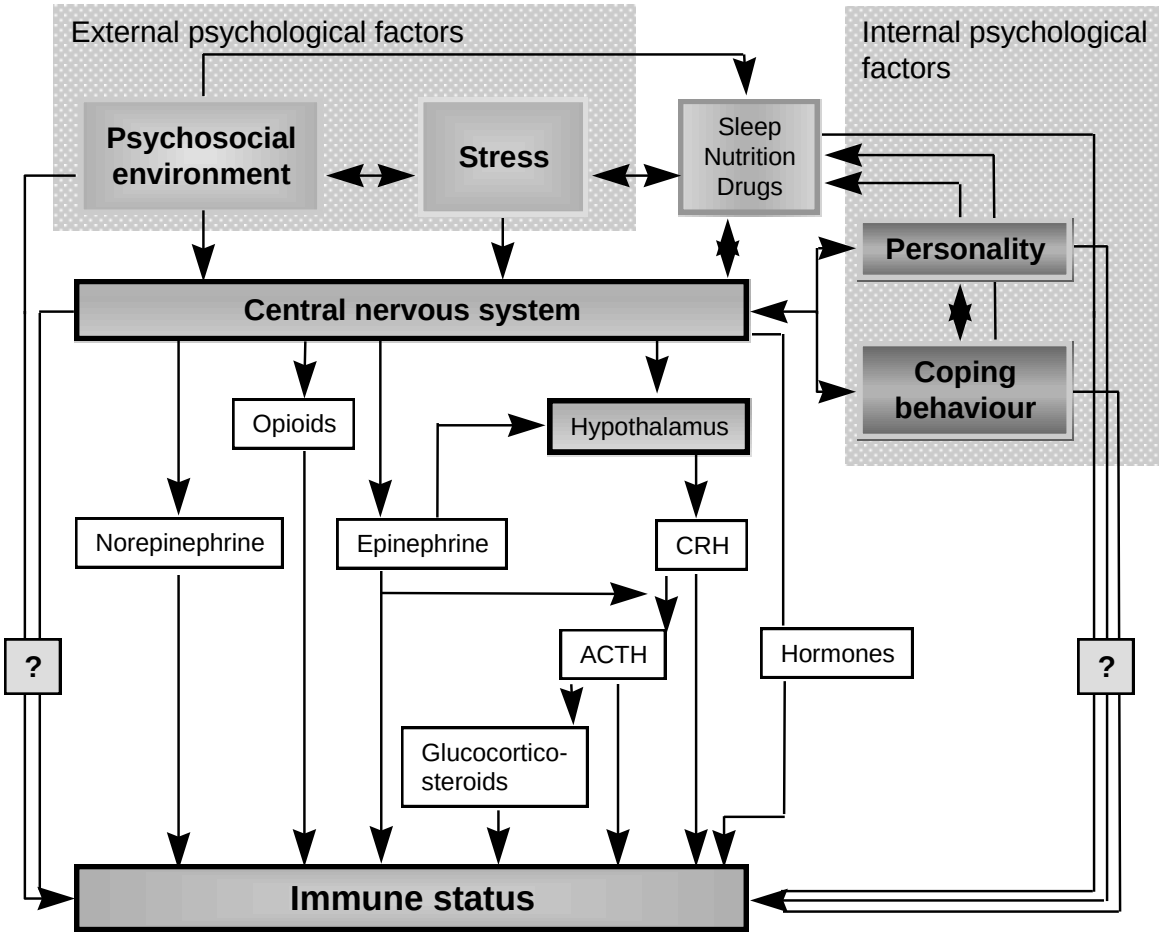
- Physical stress

Because psychological stress can be accompanied by physical stress (or vice versa) this type of stress will also be discussed here. Sport activities in healthy persons is mostly investigated. As for all above mentioned stress types, no concordant conclusions can be drawn, again because of the heterogeneity of the tests themselves and the examined persons. The best documented effect of a single physical exercise is the increase in the number of circulating leukocytes and a modification of the activity of NK-cells. Whereas an activation of NK-cells at the beginning of an exercise can be caused by increased endogenous opioids, later in time a suppression of the activity can be seen which may be related to produced cortisone or/and prostaglandins. In contrast, top athletes seem to have a higher susceptibility for infections, although no particular immune parameters could be made responsible.

Summarising it can be said that the IS is directly or indirectly under influence of many psychological factors (see Figure 2–6). What the outcome of a particular psychological factor affecting the IS in the end will be, is dependent on the psychological and physiological interactions which take place. Moreover, whether the resulting outcome is pathologically significant is even more difficult to say because no “minimal base value immune status” is defined, which has to be fulfilled to stay healthy.

Nevertheless, it cannot be denied that psychological factors can modulate the IS and may influence the onset and recovery of diseases by acting on the IS.

Figure 2–6 **Psychological factors and the immune system**



2.4.2 From the immune system to the psyche

Whereas psychological changes can modulate the IS, amongst others, by neurophysiological factors, factors produced by an activated IS can modulate the PS (behaviour, mood etc.). Activation of the IS induces the production of cytokines, who signal the disease state of the body to the CNS. As a reaction behaviour is modulated to encounter the momentary need and priorities of the situation. During an infection these behaviour modifications, known as “sickness behaviour”, may be very useful. An overproduction of cytokines however, without evident infection, may be responsible for behavioural changes in depression or chronic fatigue syndrome. Some of the effects of cytokines on behaviour will be discussed in the following.

➜ Sickness behaviour

During an infection with bacteria or viruses different cell populations of the IS produce immune regulatory factors like IL-1α or 1β, IL-6 and TNF-α or-β,. The function of these molecules can be characterised as pleiotropic and redundant, as they have influence on many different cell types and have many biological functions in common. IL-1α and 1β are expressed in different brain regions by macrophages or micro-glia cells TNF-α immune reactive neurones can be found in autonomous, neuroendocrine or behaviour regulatory brain regions.

First evidence of behaviour modulating activity of cytokines was found when patients with cancer or severe virus infections were treated with recombinant cytokines. Not only did they develop flu similar symptoms like fever, headache, muscle and joint pain, diminished appetite, lethargy, loss of interest and weakness, but also, after longer treatment, psychotic episodes with depressive or agitated symptoms. Sickness like behaviour is not only restricted to so called flu like symptoms but also decreases reaction time and the ability to solve psychomotoric tasks. Two possible pathways of behaviour modulation by cytokines have been postulated. The first is a humoral pathway: Monocytes and macrophages produce, after stimulation, cytokines. Via the blood circulation they reach the circumventricular organs and induce the production of prostaglandins, which modulate the target cells in the brain. The second pathway is neural: peripherally produced cytokines stimulate primary afferent neurones who contact to their related regions in the brain, which then stimulate the synthesis and release of brain associated cytokines, which can act on target neurones.

Whereas fever and decreased activity may serve the healing process, loss of appetite doesn't seem to be appropriate for the increased energy need during fever. Cytokines not only change food intake but also increase the endogenous mobilisation of body fat and influence metabolism. Sickness behaviour can also be seen in cancer, AIDS, depressive or anorexia nervosa patients. An over-production of TNF-α in these patients is responsible for a decreased food intake, decreased nutrition absorbency, a changed metabolism and increasing morbidity. What "benefit" such a patient has by these effects is still unclear.

The effects cytokine produce during an acute or chronic infection are also observed in patients without evidence of any infection. One of these diseases is the chronic fatigue syndrome (CSF). CSF patients report chronic tiredness and loss of motivation. In these patients increased over production of IL-6 and TNF-α after immune stimulation was found. In this case it has to be considered that abnormal cytokine-networks may as well arise by CNS produced cytokines.

➜ Schizophrenia

Apart from cytokines, the IS produces antibodies. When produced antibodies are directed against internal endogenous antigens an auto-immune disease can develop like Multiple Sclerosis or Systemic Lupus Erythematosus. Auto-antibodies have also been made responsible for the onset of schizophrenia. Although auto-antibodies directed against specific neurones or brain regions have been found, most of the collected immunological parameters do not allow ultimate conclusions.
Paranoid-hallucinatory schizophrenic episodes have also been observed in other "classical" auto-immune diseases. Whether these symptoms are immune-organic related or only a coincidence is still debated.

The overall function of all factors produced by an immune response (cytokines, neuropeptides) can now be seen as not only primarily defensive against the intruder itself, but also as behavioural modifiers to support healing and recovery. Furthermore malfunctioning of the IS may be expressed as well psychologically as physiologically.

2.5 Psycho - neurology

In addition to classical neurotransmitters, the brain functions are modulated by neuropeptides. At least up to 60 different neuropeptides are known and most, if not all, alter behaviour and mood states. Their signal specificity resides in receptors instead of the close juxtaposition occurring in classical synapses. Whereas neurotransmitters are responsible for direct transfer of a signal, neuropeptides set the "tone" of local synaptic activity by altering the effectiveness of a neurotransmitter. Precise distribution patterns for different neuropeptide receptors in the brain have been determined. A fundamental feature shared by all neuropeptide receptors is profound enrichment at a number of the same brain areas found within an intercommunicating conglomerate of brain structures called the limbic system. The limbic system (with amygdala and hypothalamus) is considered to mediate emotional behaviour. Another receptor-rich locus in the brain can be found in the brain stem where peripheral information is integrated to modulate sensory thresholds. Certain neuropeptide receptor types are not restricted to the brain and CNS but can also be found on cells of the IS (see chapter 2.3.1). Some of the psycho-modulatory functions of the neuropeptides chaired by the CNS and IS will be discussed in the following.

- Endorphins and enkephalines

β-Endorphin originates from a precursor molecule called Pro-opiomelanocortin (POMC) which is synthesised by certain cells in the hypophysis after CRH stimulation, but can also be synthesised by immune competent cells. The big POMC molecule is enzymatically split in the secretory products ACTH, α-MSH (Melanocyte stimulating hormone) and β-endorphin. Endorphins play an important role in analgesia and feelings of happiness. Hot spots with endorphin receptors have been found in the amygdala, in nuclei mediating sexual behaviour, appetite and water balance.

Enkephalines are produced in the brain, hypophysis and adrenal gland, and play a role in analgesia as well. They can bind to the same opioid receptors as endorphins

- CRH - ACTH - Glucocorticoids

CRH is the first factor in the stress induced hypothalamus-hypophysis-adrenal gland cascade and can modulate sexual, sleep and food intake behaviour as well as mood. ACTH and α-MSH both are involved in attention and arousal. Cortisone can modulate the processing of information coming from the sense organs, influence learning and memory and seems to play a role in depressive behaviour.

- Noradrenaline and adrenaline

Some neuropeptides have a dual function as they act as a neurotransmitter in the CNS, but as a neuropeptide on other structures. Examples are noradrenaline (sympathetic nervous system versus adrenal gland derived noradrenaline which promotes heart contraction or dilates the bronchioles) and vasopressin and adrenaline are involved in emotions like fear and fright.

Although many brain structures, neuropeptides, neurotransmitters, hormones and immune factors have been found to be involved in, and modulate, processes that “represent” the PS of an organism, up till now it is hardly understood why and how parts of these processes become aware, or why and how conscious experienced mental states are related to these physical processes. Furthermore, in general, the question whether the synthesis of molecules is caused by mental states or mental states are caused by the synthesised molecules is still unanswered. Although many endogenous and exogenous substances are known to change mood and behaviour when synthesised or applied, in physiological circumstances it is still a mystery, where and when the beginning of a “mood state” departs.

2.6 Conditioning of the immune system

Classical conditioning is a procedure whereby an organism is exposed to two immediately following stimuli. The first, conditioning stimulus (CS), is a neutral stimulus like a sound, taste or a visual stimulus, not connected to the process to be induced by the conditioning. The second unconditioned stimulus (UCS) follows immediately thereafter and is an exteroceptive stimulus which induces a certain physiological reaction called unconditioned response (UCR). When CS and UCS are repeatedly presented together, after a while the CS alone is able to induce the physiological response, now called conditioned response (CR). Classical conditioning differs from other learning processes in that the learning process is totally controlled by the researcher and trial and errors are excluded.

The possibility to condition the IS was first described in 1926.It was found that leukocyte numbers could be increased by a CS without any immune modulatory function. In 1975 Ader and co-workers found, more by chance, a second immune function conditioning when they experimented with conditioned taste aversion (CTA) in rats using the immune suppressive agent cyclophosphamide. Cyclophosphamide (UCS) was used together with saccharine (CS) and induces nausea. Animals conditioned this way soon refused to drink saccharine water. First when only conditioned animal became sick and a high morbidity rate occurred, the immune suppressive action of cyclophosphamide was considered responsible. Conditioned taste or odour aversion is mostly connected to gastrointestinal complaints and in humans only the thought of a certain taste or odour is enough to induce nausea or feelings of aversion. The application way of a UCS and the kind of CS determine the effectiveness of immune modulatory conditioning. Strong immune conditioning can be induced when the UCS is given per injection and the CS is visual, acoustic , tactile or chemical (taste, odour). Less effective are UCS administered by inhalation, x-ray or when it is swallowed. Both immune suppression and immune stimulation can be conditioned as well as elements of the sickness behaviour like fever.

- Conditioned immune suppression

Most immune suppressive conditioning experiments were done with the UCS cyclophosphamide and the CS saccharine which induce a conditioned reduction of the antibody titre, proliferation rate of T-cells and NK-cell activity

- Conditioned immune activation

A conditioned activation of T-cell functions could be induced in skin transplanted animals after administration of the immune stimulating drug levamisol (UCS),

- Fever

Bacterial lipopolysaccharide can be used as UCS together with saccharine water as CS to induce conditioned fever.

Conditioning of immune functions can be explained partially by stress reactions and the activation of the hypophysis-adrenal gland hormone cascade. However, they may not be involved at all when no stressing conditioning situation is chosen. Which mechanisms are involved in conditioning is not all clear yet, but conditioning of immune functions may be of great importance in the development and healing of diseases. As many neutral stimuli seem to function as a CS, unwanted immune stimulating or immune suppressing conditioning situations may be created unnoticed in daily (clinical) situations. In humans CS can even be represented by thoughts. For example in allergy the thought of an attack inducing situation or factor sometimes may be enough to induce an allergic reaction. On the other side, immune function conditioning may have great implications in the treatment of diseases where immune suppression or activation is desired.

2.7 Brain versus/compared to the immune system

Close observations of the functions executed by the CNS and the IS reveal that they have many characteristics in common. Whereas the CNS processes cognitive stimuli, the IS processes noncognitive stimuli, this processing of different types of stimuli is interrelated and co-ordinated by both IS and CNS. In addition to their own information signalling systems they both use common substances to communicate with each other, the internal body and the external world. Some of the common characteristics of both systems are listed in the following table:

Table 4 **Shared characteristics of the CNS and IS**

Characteristics	CNS	IS
morphologically cohesive	yes	partially
different cell types with different functions	yes	yes
localisation in the body	everywhere	everywhere
electrical signal processing	yes	no
chemical signal processing	yes	yes
internal and external signal transmitting molecules	yes	yes
system internal cell to cell communication	yes	yes
system external cell to cell communication	yes	yes
observer function	yes	yes
reacting	yes	yes
acting	yes (?)	?
learning	yes	yes
memory	yes	yes
internal representation of external world	yes	yes

Considering the many properties in common, the IS might be seen as a second CNS. Even though their primary functions are distinct, they function in collaboration, the CNS being as much dependent on information of the IS as the IS on information of the CNS. Assuming that all the above mentioned characteristics of the CNS are related to consciousness (CO), the question can be asked whether the IS might not as well be associated with CO.

2.8 Discussion

PNI is a discipline which studies the relation, co-operation and modulation of functions of the CNS, IS and the PS. At first the associations and connections between the CNS, NES and IS have been investigated. Today it is well accepted that CNS, NES and IS can communicate with each other by shared signal transmitting factors. Many factors

produced and processed by the three systems can no longer be seen as system exclusive. Although much harder to understand, the network of CNS, NES and IS can offer additional information on the how and why of processes in disease and healing.

Which importance the PS has in PNI is still a topic full of controversies? Although many observations in the daily (clinical) grind have shown the importance of positive mental states and feelings in the process of healing, no satisfactory experimental design seems to exist which can offer answers on how moods and feelings influence the onset or cure of diseases by altering the IS. The biggest problem in this part of PNI research may be, that so far, it is not clear how conscious and/or unconscious psychological processes take influence. Even though experiments with psychotherapy, meditation or positive thinking, for example for cancer patients, to increase immune functions show encouraging results, nobody can measure individual internal thinking or feelings. At this point the body-mind (BM) problematic enters the discussion.

Up till now the BM problematic did not receive much attention in PNI research. As long as the relation between body and mind is unsolved, PNI research will not be able to find definitive answers on the role of the PS. Regarding the similarities between the CNS and IS, as postulated in chapter 2.7, one might speculate that CO and un-CO are as well related to the IS, as they are considered to be related to the CNS. The PS is then also directly associated with the IS, without the need to make a detour by the CNS and many controversies found in measured physical factors, assuming only a PS $\Rightarrow$ CNS $\Rightarrow$ IS pathway, might be elucidated.

The following chapter will discuss the BM problematic in more detail, in order to obtain more insight in the PS $\Leftrightarrow$ CNS and possible PS $\Leftrightarrow$ IS relations

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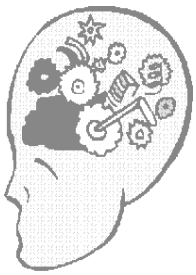

3. Body and mind

3.1 Introduction

As PNI research has shown, health and disease are not only under control of body processes, but are also influenced by mental states and psychological factors. Exactly these mental and psychological factors are the difficulty in PNI research, as they can less well be standardised and, as something immaterial, hardly be measured in a test tube. In addition, for most of the mentioned psychological factors in PNI research (stress, emotions, coping behaviour, depression etc.) it is hard to define whether they are consciously experienced or not, and verbal reports of sensed mental states therefore might be incomplete.

The question, whether mind or mental states[2] are only products of brain processes, or brain processes are only the (end)- product of mental states, and how, why and which of these processes become conscious, or whether mental states themselves can influence brain processes, is still unanswered. In the following chapters some of the approaches in the body-mind theories will be reviewed and their consequences for PNI research discussed.

3.2 Monism

The mainstream in consciousness (CO) theories tries to explain how mind or mental states arise out of brain processes and how these mental states reach or obtain CO. The theories vary from simple “the mind is what the brain does” to the introduction of new physical. What all theories have in common is the idea that mentality is at bottom physically based and neurophysiology in the end will explain the mind. In brief monistic ideas can be summarised as:

- The mind is identical with brain processes

The standpoint, minds are simply what brains do, implies that mental states are identical with the processing of different inputs a brain receives externally (visual, auditory, tactile, olfactory and taste) and internally (neuropeptides, hormones etc.). The art a certain brain reacts on a given input is dependent on its structure which is defined genetically.

[2] In the rest of the text with “mind” or “mental states” are meant all phenomena related to consciousness. They include properties like perception, awareness, thoughts, feelings, memory, qualia, self-consciousness, intentions, free will etc.

- The mind is a function of brain processes

Functionalism regards the mind as realised by the brain. Mental states themselves are not identical to brain processes, but are realised by them. For every mental state there is a neurophysiological correlate located in a certain brain area or neural network.

- The mind as an emergent or supervening property of brain processes

The idea of emergence or supervenience takes in the position that mental states appear as a new characteristic of all physical brain processes, but are not identical with the sum of those processes. The theories assume a layered model where at each level there are properties, activities, and functions that make their first appearance at that level. What the outcome of a higher level will be, given a certain lower level, can not be predicted as it is not identical with the sum of the properties, activities or functions of the lower level. Mental states are "second-order" properties defined over first-order physical properties. In contrast to functionalism, where mental states can be reduced to neurophysiological processes, the idea of supervenience or emergence does not allow reductionism, simply because $1+1 \neq 2$ but may be anything.

What all monistic concepts have in common is the dependence of mental states on the physical, or the physical determines the mental. The mind, being in one or the other way a product of what the brain does with all incoming internal or external stimuli, therefore does not seem to be able to function as an input itself. With other words phenotypes can or do not affect genotypes. The consequence this has for PNI is that mental states themselves cannot influence body functions. That a particular mental states is found together with an immune modulatory processes is only because the evoking stimuli (input) result in a specific mental state as well as in a certain immune modulation, but the mental state itself cannot be responsible for the immune modulation, as both mental state and immune modulation are "output".

3.3 Dualism

Dualistic theories picture the world as consisting of two independent spheres, the mental and the material. Both spheres can interact causally with each other, but each domain is ontologically independent, and can exist in total absence of the other. Dualistic ideas can be found far back in history and in many cultures. In the following some modern dualistic opinions will be described.

- Psychones

According to John Eccles, quantum physics play a key role in mental states. Mental events change the probability of a vesicular emission to happen, generated by a presynaptic impulse. Special areas in the cortex of the brain (bundles of ascending

dendrites of pyramid cells called dendrones by Eccles) are reciprocally linked to a certain mental event. The whole range of possible mental states consists of elementary, uniform mental events which are called psychons. For every psychon a bundle of dendrits exists (called dendron by Eccles), whereby the psychon can change the probability of the nerves in the dendron to become active/reactive or not.

- Hardware and software

Daniel Dennett compares brain and mind with hard and software. The “hardware brain” makes it possible that the “software mind” can be run on it. Without the hardware the software cannot be run and the output of the software not be realised. Different software may run on the same hardware and the other way around. The outcome of the running software therefore is only dependent on the software and not on the hardware it runs on.

- Quantum mechanics

The major features of the quantum theory include wave/particle duality, the (Heisenberg) “uncertainty principle”, superposition, randomness or a-causality, and non-locality. The duality of the theory implies that a particle exists in many possible states (superpositions) but only one state can be observed at a time (collapsed superposition). Many of these features can be applied to the BM problematic: the “matter-like” and “thought-like” aspects of the mind/brain. CO is associated with the self-collapse of a quantum superposition (or wave function collapse) which is supposed to happen in different biological structures like microtubuli or ion channels of neurones.

Dualistic conceptions share the assumption that mental states can influence the brain. The above mentioned models can be of interesting significance for PNI. First the mind is thought to be an independent component effecting brain functions, which then can result in immune modulation. Secondary the postulated effects the mind has on biological structures, such as microtubuli or ion channels, might happen as well in other cells then neurones, thereby connecting the mind to the whole body instead of only to the brain. What these models do not explain is where these mental states originate, and how external and internal stimuli modify mental states. Although for example stress as a mental state influences what the brain cells (and maybe all other cells of an organism) do, which may result in indirect or direct immune modulation, from these theories it is not clear how stress becomes a mental state in the first place.

3.4 Forces and fields

Libet and Popper formulate and discuss a new aspect of the theory of mind. This theory is partly based on earlier developed interactionistic theory. It takes as its point of departure the observation that mind and physical forces have several properties in common, at least

the following six: both are (i) located, (ii) non-extended, (iii) incorporeal, (iv) capable of acting on bodies, (v) dependent upon body, (vi) capable of being influenced by bodies. Other properties such as intensity and extension in time may be added. Because of some physical properties of the brain, including the three dimensional structure, force fields like electromagnetic fields, are probable to occur. Whether other (yet) indiscernible fields may occur is an open question. Interesting features of the mind being a field or force is, that body and mind are separate individual entities, capable of influencing each other but also depending on each others existence. Although a field or force theory still does not explain why and how mental states are experienced, the model would at least mean that mental states can be influenced by incoming internal and external stimuli, as well as they affect (directly or indirectly via the CNS) the bodily output of these stimuli. The model integrates monism and dualism and assumes a dual directed cause and effect pathway (feedback loop) as it is seen in most of the biological interacting systems.

3.5 The “self” and the “I”

Beside the unsolved problem of how CO “arises”, the question how far CO itself is responsible for immune modulation can be asked. Experiments done by Benjamin Libet have shown that brain activities become “delayed” conscious. At least 0,35 sec brain activity is going on before these activities become conscious, or that the conscious decision to undertake a certain action occurs around 0.35 sec after the time the brain became active, Libet called these brain activities readiness potentials. CO is projected back in time and according to Libet CO cannot initiate an action, however, the decision becomes conscious 0,2 sec before the action is carried out. To save the problem of free will Libet postulated that CO can stop the ongoing readiness potential in these lasting 0,2 sec before the readiness potential is set into action(veto theory).

The experiments of Libet together with the phenomenon of subliminal perception and the limited capacity of information quantity storage per time unit of the CO, led Tor N⌀rretranders to describe that a person consists of two “persons”: the “self” and the “I”. According to him the “self” (or the readiness potentials according to Libet) is most of the time in control of all actions, only when time to consider is available the “I” (the conscious veto right of Libet) may take over control. Although the “I” may ignore the existence of the “self”, it has to accept that other forces then its own are on work part (or even most) of the time. The problem is that the “I” cannot accept that the “self” is not predictable, messy, fast and powerful. When the “I” tries to control the “self” it may disturb the healthy adequate reasonable actions the “self” is producing.

Thoughts on the existence of a “self” and an “I” are important for PNI research. If the PS is playing a role in illness or the process of healing, the question arises whether it is the “self”, the “I” or both which represent mental states. Is the “self” responsible for mental states and the “I” virtually an observer with low influence ?, or are mental states caused by the “I” thereby negatively disturbing the actions of the “self” ? Would the body be better off if the “I” did not take too much influence and the “self” could develop “self” healing actions ? But not only these questions are interesting in case of possible psychological therapeutic interventions in healing, it has to be considered if it is at all possible to influence immune functions by the conscious “I”, or if it is possible to reach and influence the “self”.

In addition it has to be taken into account that thoughts on the “I” and the “self” depend much on cultural traditions, consequently influencing the attitude towards the role of the PS in illness and health. In western cultures it is hardly accepted that the “I” might not be as powerful as wished, and many actions may not be initiated by a conscious “I” at all. Other cultures however may accept the power of the “self” and even try to get free from the “I”.

3.6 Discussion

Although the above mentioned theories on CO are far from complete the short résumé shows that different theories have various consequences for PNI. Thinking over these consequences might give new insight in what, where, why and how CO is. Even though PNI takes in the position that the PS of a person or psychological factors can influence physiological body processes, it seems that the conscious “I” is only partially in control. Whereas most of the body functions and actions never reach CO it might be questioned if CO itself can reach or influence these actions. Maybe it is better not being aware of all those processes, as it may be better that not all physiological processes can be influenced by the conscious “I” and one might think oneself to death.

On the other side it cannot be denied that physiological processes are under influence of more than only the matter they are made of. If not the “I” maybe the”self” could have influence, which may be partially conscious and mostly unconscious. If the “self” should be thought of as a monistic, dualistic or force/field theory may be argued. Important for PNI research however is to consider if immune modulation by psychological factors is at all a conscious process or is only unconscious or maybe both. In case psychological factors or mental states are made responsible for the onset of diseases or are used as

additional therapies in the process of healing, the attention on these topics should be intensified.

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www 9 Craig Delancey, Mood and the representational theory of consciousness

http://phil.indiana.edu/~cdelance/cve/cve_mrtc.html

www 10 Daniel Dennett, Facing backwards on the problem of consciousness

http://www.tufts.edu/as/cogstud/papers/chalmers.htm

www 11 Fred Dretske, The mind's awareness of itself

http://www.nyu.edu/gsas/dept/philo/courses/consciousness/papers/dretske.html

www 12 Fred Dretske, What good is consciousness?

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www 14 William James, Does `consciousness' exist?

http://wiretap.spies.com/Gopher/Library/Classic/empiricism.txt

www 15 Peter Lloyd, Is the mind physical? Dissecting conscious brain tissue

http://easyweb.easynet.co.uk/~ursa/philos/phinow2.htm

www 16 Marvin Minsky, Minds are simply what brains do

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www 17 Bruce MacLennan, The elements of consciousness and their neurodynamical correlates

ftp://cs.utk.edu/pub/maclennan/JCS2/JCS2.html

www 18 Josh McDermott, Global workspace theory: Consciousness explained?

http://hcs.harvard.edu/~husn/BRAIN/vol2/consciousness.html

www 19 John Searle, The problem of consciousness

http://cogsci.soton.ac.uk/~harnad/Papers/Py104/searle.prob.html

www 20 Aaron Sloman, Notes on consciousness

http://www.cs.bham.ac.uk/~axs/cog_affect/Aaron.Sloman_consciousness.ps.Z

[3] No guarantee can be ensured that the listed pages can be found under the cited internet address in the future.

4. Mental states; emotions, moods, beliefs, hope and will

4.1 Emotions and moods

Emotions and moods are conscious mental states which are believed to play an important role in the onset and healing processes of diseases. Whereas neural correlates for emotional states are partially defined, no such correlates have been defined for moods. Certain brain centres can be located which are activated and involved in emotional processes. How emotions become conscious and are experienced is as unknown as for other mental states. As already discussed in the above chapter on consciousness it has to be carefully thought about whether emotions themselves influence body functions, or whether emotions are an expression of physical (CNS) processes occuring simultaneously with or even because of health changes. Because of the relative well defined neurophysiological substrate of emotions, the relation between emotions and health (or the IS) can be studied in more detail than the relation of mood and health.

4.1.1 Definitions of and differences between emotion and mood

Mood and emotion are two words that are sometimes used interchangeably and are used alike to refer to certain aspects of affect. Different definitions are used for emotions and some of the different characteristics of emotion are listed in the following:

- Emotions can basically be divided into two groups, 1. those which are involved in avoidance, withdrawal, negative behaviour, and 2. those which are involved in attraction, approach or positive behaviour.
- Emotions can be “basic” innate, genetically determined or secondary “learned” as a combination of the “basic” emotions.
- It is the appraisal, not the stimulus event, that is crucial to understand which emotion occurs
- It is the possibility to express a certain behaviour that determines which emotion occurs
- It is the probability of need satisfaction that determines the emotional outcome of a stimulus.

Emotions seem to occur when something unexpected happens and are in the first place related to external stimuli. Stimuli can evoke emotions directly, or indirectly by activating memory. The intensity of emotions is partially dependent on the personality and the genetically determined excitability.

Although emotions and moods have many similarities, in the literature they are defined as two different mental states. Moods are referred to as having different/opposite characteristics as those mentioned for emotions which are listed in Table 5. Similarities

between emotion and mood are that they may “feel” the same and that both can be influenced by internal (neuropeptides, hormones) and external (drugs) chemicals.

Table 5 **Differences between emotions and moods**

	Emotion	**Mood**
Duration	short	long
Stimuli	event related object orientated external	not event related not object orientated internal (?)
Expression	by the autonomous nervous system: facial, heart beat etc.	not necessarily expressed
Interaction	1. emotions may facilitate the development of mood 2. One emotion inhibits other emotions	1. mood can alter the threshold for the elicitation of a certain emotion 2. Different moods may be experienced at the same time
Behaviour	immediate adaptation to environment	appraisal of the existential background of life
Bias	action	cognition

4.1.2 The physiology of emotions

One of the brain centres associated with emotions is the limbic system including thalamus and hypothalamus and in particularly the amygdaloid nuclei (amygdala) and their interconnections with prefrontal cortical regions. Neurologists found that when they used electrodes to stimulate the amygdala they could evoke a whole array of emotions. In addition many neuropeptides and hormones can influence emotion. Most of the literature describes that specific biological changes accompany and provide the substrate for different emotions although the question remains unanswered whether the autonomic nervous system will show emotion-specific pattering. A summary of the physiological changes accompanying, causing and/or influencing emotions is listed below:

Autonomous nervous system induced:

- facial expression
- heart rate
- muscle tone
- vasoconstriction or dilatation
- sweat production

A great number of neuropeptides placed into the brain have been found to modify emotive behaviours and emotive states or are elevated during an emotional experience:

- CRF and ACTH are strongly implicated in the genesis of anxiety and fear
- vasopressin and testosterone in aggression
- opioids in joy and happiness

In addition, in the limbic system highly enriched areas with opiate receptors have been found.

One of the problems physiological data have not solved is that different experienced emotions may be accompanied by similar physiological changes. For example excitement because of an appointment with the dentist and excitement because of an appointment with the person one is in love with may result in very similar bodily changes (heart rate goes up, sweat production is increased, the stomach contracts etc.) although two completely different feelings are involved. Only Levenson found some differences in heart rate between disgust and anger, fear and sadness and skin temperature differences between anger and fear.

4.1.3 Emotions in health and disease

The influence emotions may have on health and disease can be directly induced by the physiological factors involved or indirectly when the expression of emotions is suppressed.

➜ Direct influences

Physiological changes (increase or decrease in neuropeptide concentrations and the above mentioned autonomous nervous system actions) occurring after an emotion evoking stimulus modify body functions. Many of the neuropeptides involved in emotions also have immune modulating effects (see 2.3 page 30). Because emotions are defined as rather short lasting events (in the range of seconds to minutes) the question arises whether the changes in neuropeptide and hormone levels are of any relevance. In contrast, on-going stimuli evoking a continuous flow of emotions may have immune modulating effects. When emotions result in a mood change, such a mood may last for

hours, days or even longer. Moods however may no longer be accompanied by physiological changes and the influence of moods on health and disease may be caused by behavioural changes influencing body functions such as sleep deregulation, food intake and others.

➜ Indirect influences:

In order to maintain the social order, cultural convention, interpersonal bonding, power and influence, control of emotion is ubiquitous, although the psychological and physiological consequences of inhibiting the free flow of emotions is depicted as dire and unhealthy. Levenson et all have investigated the effects of the voluntary suppression of visual expressed emotions. The results showed that suppression of non-verbal visible signs of emotions produces heightened activation of the sympathetic branch of the autonomous nervous system, even prior to the inhibition. Although no visible signs were expressed the feeling of the emotion remained. Suppression and control of the expression seem possible, although the physiological changes accompanying the emotion are not inhibited, in contrast they even seem to be increased as "work" has to be done to suppress the expression. Suppression of emotions may become unhealthy when the physiological arousal is in excess of the metabolic demand. For example when aggression is felt and the emotion can result in an aggressive behaviour the hysiological changes serve the behaviour and the released energy is used. In contrary when the aggressive feelings have to be hidden this energy still seems to be released but cannot be used.

Not only may emotions influence health, factors released during diseases can trigger emotions. Cytokines and factors produced by tumour cells may induce emotions such as fear, anxiety or aggression which, when they are prolonged, may induce moods of helplessness and hopelessness.

4.1.4 Control of emotions

According to LeDoux innate emotions are a product of evolution common to all members of a species occurring in regard to stimuli for which the species has developed response strategies. These emotions are involuntary; it is possible to abort but not to inhibit the initiation of such emotions. The amygdala can trigger emotional reactions before the cortex has fully processed the triggering input. The emotional response seems to be a front line reaction that springs quickly into place before rational deliberation has had time to function. Because of the different neural networks involved in emotion and conscious reasoning responses, emotions seem to short cut the circuits for reasoning and thereby bypass free will. Emotions seem "to happen" and can't be called forth on command, nor can they be terminated simply by choice, they only may be avoided by eluding provoking

stimuli. Whereas the expression of an emotion can be suppressed, the feeling cannot. Emotions may be remembered but the memory itself is not the same feeling as during an experienced emotion. In relation to the “self” and “I”, emotions seem to be a part of the “self”. The “I” can suppress the expression of or actively avoid, but cannot initiate, inhibit or terminate, emotions.

4.2 Beliefs, hope and will

In contrast to emotions, biological correlates of belief, hope or will are less well investigated and therefore cannot be described in terms of neurotransmitters, neuropeptides or hormones. Still, these mental states may be experienced as strong as, and in addition to, emotions and may have similar positive or negative influences on health and disease. Even though modern biomedicine may deny a biological influence of belief, hope or will because these immaterial mind states are not thought to be able to have any influence on physical processes, daily medical cure, even in modern western medicine, often encounters these mental states.

Belief, hope and will are interrelated mental states and personally as well as culturally determined. Specially for belief it is difficult to give a clear definition, but at least two distinct things can be meant: a) to assume something is true or b) to know for certain something is true. The first category implements religious beliefs or wishes for something to happen in the future (I believe in God, or I believe I will get better) and may be seen as a mixture of hope, uncertainty and confidence. The second definition is more rational and implies all those statements based on proof (I believe that the earth turns around the sun, or I only believe it when I have “seen” it myself). Hope can be seen as a weaker form of belief (a) and implements desires and wishes for something to happen. Hope is directed towards an uncertain event or situation. The driving force to achieve something hoped for or believed in is uttered in the will.

In general beliefs are very subjective and can be totally irrational. For research the only available information on an individual’s belief can be obtained verbally, which cannot be proven to be”true”. Another problem is to distinguish between a belief and hope. A belief implies a subjective personal certainty, knowledge or confidence, whereas hope embodies uncertainty, but both feelings may be interchanged and mixed during verbal expression. Beliefs may exist on a subconscious passive level without attaining awareness, hope and will in contrast are active conscious feelings or acts and even may be directed towards the opposite of what is believed. In context with the different consciousness theories beliefs, hope and at most (free) will are hard to fit in and research on brain processes during a

mental act of believing or hoping (like for visualising, remembering, speaking etc.) does not seem to be available.

In the next chapters some aspects of belief (religious and non-religious) described in the medical literature will be summarised.

4.2.1 Religious beliefs

The best overview of religion influencing health and morbidity is given by Levin. The effects religion can have were investigated in two types of settings namely religious affiliation and religious involvement (e.g. frequency of religious attendance). The overall results point to a mostly salutary or protective epidemiological effect of religiosity. Some of the proposed hypotheses to explain these findings are:

- health-related behaviour including special diets, less drinking or smoking, sexual restrictions etc.
- psycho-social support
- psychodynamic benefits like physiological responses to positive emotions during worship or prayer
- the positive effects of a religious world view as in the fostering of learned optimism and salutary health beliefs

Religion in general includes a “meaning of life” and implements feelings of comprehensibility and why challenging events make sense. In case of negative situations or disease religious beliefs may call forth less negative or frightful emotions and stress. The health protecting effects of positive emotions and decreased stress can have biological consequence like immune modulation as described by PNI.

Although religious beliefs may have salutary and protective influences on health this does not mean they can heal and as Levin writes “The clinical value of simply being religious has not been studied, and its therapeutic efficacy as a specific strategy for curing diseases seems implausible”. The only substantial body of scientific evidence concerning the effects of beliefs in healing are indirect and come from studies on the therapeutic effect of prayer and directed intention. On a physiological basis prayer may contribute to physiological changes as meditation does, like decreasing stress factors, bring about positive emotions and in general calming down body (metabolism or the fight-or-flight reaction) and mind. In spite of the mostly failing scientific physiological measurements for “a state of religious belief”, people experiencing these beliefs seem to benefit from these mental states, whether direct or indirect, during health or disease.

4.2.2 Non-religious beliefs

Literature (scientific) on the effects of non-religious beliefs in disease and healing is hardly, if any, available unless in the case of literature on placebo and the placebo effect (chapter 5). Going through a disease individuals may experience both kind of beliefs as described in chapter 4.2 depending on the severity and curability of a disease. Whereas trivial diseases or injuries like a cold, flue or broken leg may not evoke strong beliefs as they will be cured for sure, on the other side diseases with a high mortality rate or uncertain outcome like cancer may arouse strong beliefs. These beliefs can be inward orientated and be independent of what therapy is chosen, or they may be outward orientated and can motivate an individual to choose a certain therapy.

The only available signs that beliefs and hope may influence the course of a disease are observed and thought to be demonstrated in “miracle” healing in cancer (and other) patients, however, most of these observations are made in (scientifically) uncontrolled individual cases without scientific evidence. In spite of the few medical scientific reports on the influence of beliefs, non-scientific reports and writings are manifold (specially on the internet or world wide web) and insist on the power of belief in disease and healing. Without defining what belief is or what its biological consequences could be it is stated for example that -the belief in disease is the determining factor why some people do get sick and others don’t under the same circumstances-[4].

4.2.3 Belief and will

In addition to beliefs and hope, the will to stay healthy or to be cured seems to play a role in the healing process. Again scientific literature on this subject is rare. As for beliefs, biological correlates for a “state of will” have not been investigated and different theories on consciousness have the hardest problem implementing “free will”.

In some religious contexts, can be external: it is the will of God or the Gods, that something is the way it is or how it will change. Responsibility for a certain situation is placed outside the individual and whether one will be cured or not is thought to be dependent on the will of the God(s). Non-religious beliefs can come along with a strong will to realise what is believed in and the responsibility for achieving this goal is taken personally. Which role a will to get better and feelings of (taking) responsibility for the own healing process play can only be judged subjectively and can hardly be measured in standardised objective values. Specially in alternative and complementary therapy forms,

[4] A search with one of the search machines on the internet like Altavista or Yahoo, using the words “healing or health and belief” results in more than 1000 articles concerning this subject.

but also in Asian medicine, in addition to the visible and technical external aspects of healing the vital factors in the healing process are thought to include belief, confidence and the will and passion for living (. 1, footnote 4 page 49)

4.2.4 Belief, hope will and the “self” and “I”

Beside the above given definitions of belief there might be another aspect to it. It can be hypothesised that belief can be divided into external orientated (to believe in God or that the earth turns around the sun etc.) and internal orientated. With internal orientated belief is meant that an individual (sub)-consciously has “knowledge” of its state of being (I believe I am healthy or will get better), People with severe life threatening diseases sometimes seem to be aware of their inner situation, even though all the odds are against or for them and external orientated beliefs, hopes and will can be opposite directed to such inner beliefs. Assumed, an individual’s consciousness is based on a “self” and an “I”, it may be questioned whether internal orientated belief or “inner knowledge” is part of the “self”, whereas external orientated belief and hope are constructs of the “I”. In a world where belief in general has lost its power and acceptance in society, inner beliefs are not trusted and allowed to believe in anymore. The “I” is supposed to believe in therapies and treatments whereas the “self” might know better what should be done to get better. Healing then may be achieved when the “self” is allowed to take over and ordain handling, and treatment supports the “I” and the “self” to harmonise and be unanimous.

4.3 Discussion

Mental states are difficult to define situations because of their subjectivity and may involuntary happen (emotion or depression) or can be actively and voluntary “induced” (belief, hope, will). They can be less well standardised as physiological properties and therefore are hard to “measure”. Although it can be assumed that all mental states have a physiological correlate in the brain and/or body, only some of them can be evaluated in a “material” manner (as for stress or emotions) but for none of these states it is clear whether the physiological correlate is caused by the mental state or the other way around. As far as evidence for a “material” correlate of the mental state is lacking it is often assumed to be of no relevance for body processes. Although PNI research has shown that at least some mental states can be of influence on body functions, this research restricts itself to physiological measurable and mostly negative (stress, depression etc.) elements and the effects of “positive” mental states such as will, belief and hope are less well investigated or ignored. Maybe future PNI research will also examine these “positive” mental states and find physical components involved in and modulating the IS and health.

In spite of an overall missing scientific biomedical interest in the healing properties of these mental elements, the daily practice shows that people rely on them and search for acceptance. Alternative (ancient and new) or complementary therapies implementing or completely relying on (because of lack of scientific evidence for their mechanisms of action) elements like belief become more and more popular. In the USA institutes like the “Body/Mind Medical Institute” (Boston, see. 98) try, in addition to conventional therapies, to involve (as they say) the power of mental states in the healing process.

Maybe some mental states have no biological correlate at all and are real “mind” phenomena. Consequentially, implementing these immaterial “mind” phenomena in scientific medical research might someday “prove” their importance in and influence on body functions. In addition modern biomedical science should and could reconsider to what extent their physically based scientific thinking is influenced by “beliefs” themselves and why an immaterial “mind” should not be of importance.

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5. Placebo

5.1 History

The word placebo roots from the Latin language, meaning “I shall be pleasing or acceptable”, and refers to the wish and will of a person, who seeks for the physicians care and help, to be healed. Although throughout history, medicine has relied on treatments without any modern scientifically proven “effect”, the word placebo has become a negative meaning in modern times. Until the mid-1800s physicians as Richard Cabot used placebos “acting upon a patients symptoms through his mind”. After Robert Koch and Louis Pasteur demonstrated that specific bacteria could cause specific diseases which could be cured by specific medication, medicine increasingly disregarded the importance of placebos, beliefs and BM interactions. The development of modern biomedicine, the industrial production of medical drugs and legalisation and registration of drugs by governmental institutes, required the demonstration of safety and effectiveness of a drug. This requirement included that the effect of a drug could be distinguished from other influences such as spontaneous changes, the course of the disease, “placebo effects” or biased observations and that differences in outcome among patients, concurrently randomised to therapy, should not be due to personal beliefs, secondary interests, and/or prejudices of patients, investigators or sponsors. According to these needs “double blind clinical trials” were designed using a substance (like physiological saline versus morphine) or therapeutic procedure (like a sham operation) without any specific activity as “negative control”. The observed changes in the physical (and psychic) condition of (test) patients in the “negative control group” became known as the placebo effect (PE) and were rather seen as tiresome then regarded as being interesting. First in the 1940s and 1950s the large-scale use of placebos in clinical research emerged, simultaneously with scientific knowledge pertaining to the PE.

5.2 Definition

With increasing interest in placebos and PEs a great number of studies were performed and evaluated trying to show the impact they had on the evaluation of drug responses, their power or their non-existence. Because of the many different definitions of a placebo or PE, attained results differed among studies. The following list of placebo or PE definitions elucidates the problem.

Placebo definitions:

1. a placebo is an intervention designed to simulate medical therapy but not believed to have a specific effect on the illness or condition to which it is being applied
2. a placebo is any therapeutic procedure (or component of a therapy) which is given deliberately to have an effect, or unknowingly has an effect on a patient, symptom, syndrome, or disease, but which is objectively without specific activity for the condition being treated
3. a placebo is a medical procedure that has no direct physicochemical effect on the condition in question
4. a placebo is an imitation of a treatment

In general a placebo is the non-specific arm of a specific treatment. This dichotomy however has its problems. As an imitation a placebo always contains some substances (where the placebo replaces drugs, or in case of sham operations anaesthetics which still have to be applied) or manipulation and its non-specificity can only be determined negatively by exclusion of what is specific in the case in question, which however can never be acknowledged for certain as not all specific modes of actions may be known.

In case of the PEs there are again different definitions in use:

1. a PE is the symbolic significance of a treatment in changing a patient's illness and refers to any change in behaviour or conditioning following the administration of a placebo which is not attributable to specific pharmacological or physiological properties
2. a PE is the total of unexplained consequences of administering placebos as well as active treatment
3. a PE is the therapeutic change in a patient's condition that is causally connected to the patient's personal awareness of being in a clinical situation

Kienle et al however doubt that any PE exists and call it an illusion. According to them what is called a PE by others is no more than a) the natural history of the disease, b) observer bias, c) patient bias (such as obliging reports, conditioned responses or neurotic or psychotic misjudgements), d) no "real" placebo administered (psychosomatic and psychotherapeutic effects), e) the placebo has an unknown specific effect, and others. This different opinion however relies much on the used definition. If an inhaled saline aerosol can provoke an asthmatic attack or reduce bronchospasm, as good as a real allergen or an specific effective medication, dependent on what the allergic asthmatic test person is told, saline aerosols can be called a specific pharmacological substance and therefore no PE occurs but a real therapeutic effect, or as "negative control" a placebo with its PE. The real placebo in this case may be "what is told" and the PE "what is believed it does".

In a strict scientific sense a placebo does not exist as any substance or manipulation may have some physiological effect as the dummy sugar pill, pure water, other solvents or sham treatments are somehow processed by the body (and mind). On the other hand it cannot be denied that other factors than only the specific drug or treatment are involved in the effectiveness of it. Even if they are only due to the natural history of the disease, observer and patient bias etc. it may be questioned how these effects can occur without the administration of the so called specific drug or treatment, and what the “real” effectiveness of drug or treatment administration basically implies.

5.3 Methods and results

Results on placebos and PEs in the first place are obtained indirectly by clinical placebo controlled double blind trials, which means that patients and administering physician do not know whether they receive or administer the “effective” or “non-effective” therapeutic substance. In this case a placebo group is the “negative control” group which may only differ from the treatment group in one, and only one, aspect namely the applied drug. Secondary PEs themselves may be studied. There are two possible settings for studying the PE itself: a) a test group of patients receives a placebo and a control group receives nothing but does get all other medical attention the test group gets; PEs still may be observed in the control group, and b) a test group of patients receives a placebo and the control group is a “no treatment”, “no contact” or “custodial treatment”. The idea behind the experimental setting of b is to eliminate PEs caused by psychological factors of a treatment, however such a setting is very difficult to constitute. It has long been known that participants in drug trials or research studies get better faster and have better results than other patients (Hawthorne effect) and therefore the main problem in such a setting is that the control group is not in a clinical setting in contrast to the test group.

PEs have been demonstrated in many different clinical settings and for psychical problems as well as for physical problems. In the study of Beecher 26 studies comprising more than 1000 patients suffering from a variety of disorders a mean PE of 35.2% ± 2.2% was calculated. A list of observed PEs is given in Table 6.

Table 6 **Observed placebo effect rates**

Treatment for:	Treatment	PE rate in %	Reference
Analgesia	medication	35%	. 101
Duodenal ulcer	gastric freezing	24-64%	. 104
Irritable bowel syndrome	medication	40-70%	. 104
Bronchial asthma	aerosol inhalation	20%	. 107
Depression	medication	30-70%	. 112
Panic disorder	medication	34%	. 112
Angina pectoris	sham surgery	100%	. 115
Herpes simplex virus	ineffective treatments	83-100%	. 115

Not only can placebos bring positive effects. A so called nocebo effect can be seen when patients are told a certain treatment will cause side effects such as dizziness, headache or nausea. Even when received a placebo, some patients report these side effects . Another observed kind of nocebo effect was seen when asthmatic patients were given a true bronchodilator but told it would have a bronchoconstricting effect. They responded 50% less with bronchodilation as a control group knowing they received a true bronchodilating drug.

5.4 Explanation and requirement

PEs are explained psychologically as well as physiologically as listed below:

1. Decreased anxiety. Placebos seem to be most effective for highly anxious subjects. Reducing anxiety and stress, caused by or as a component of, the placebo effect may have physiological effects and increase for example immune functions as described by PNI research.
2. Expectations. Being in a clinical (test) situation, expectations of improvement may be high(er), small improvements are noticed and can lead to beneficial behavioural changes. Expectations may increase the will to get healthy and change the judgement of experienced symptoms.
3. Learning. Past treatment responses may influence patient's responses to subsequent treatment. When such treatments are associated with certain performances these performances may lead to conditioned learning (see chapter 2.6 page 42). The reiterated application of a (placebo) treatment may induce a conditioned response. As in classical conditioning experiments some placebo treatments seem more powerful than others (injection or pills) and also form, taste and colour of medication can

influence the effect. The fact that babies without “therapeutic experiences” do not respond to a placebo treatment supports the conditioning theory.

4. Endorphins. It has been suggested that endorphins are involved in the PE. The release of endorphins may explain mood and behaviour changes (less anxiety and stress) and is immune modulating which may lead to improved health.

The above described models are not mutually exclusive and all four of them simultaneously may play a role. Although the functional mechanisms of PEs are still uncertain one essential supposition to evoke a PE is indispensable: patients have to be conscious, a comatose patient does not respond with a PE. Other PE stimulating factors are the providers behaviour (persuasive, interest, sympathy, empathy), positive beliefs and expectations in both patient and physician, a good physician - patient relationship and type, dosage, form, colour and the regular disciplined intake of drug.

5.5 Ethical considerations and implication

The use of placebos involves two major ethical problems. In double blind placebo controlled medical experiments patients (and physicians) are deceived and patients may be withheld a true effective medical treatment. Because a PE is based, at least partially, on beliefs it is difficult to avoid deception, however even patients who have been told they received a placebo, may react positively and “belief” they received a true drug. As long as the therapeutic effect of a new component is unknown, placebo controlled experiments are essential and the ethical problem is reduced to whether one should deceive someone or not. In the case of placebo experiments to test for PE versus a known medication the second ethical problem may arise. The general problem of placebo research is that it contains elements which cannot or are not considered scientific. As long as “belief” and “faith” remain unscientific subjects these ethical problems may not be solved.

Whatever definition is given to the PE (strict scientific or broad folk meaning) therapeutic interventions seem to consist of more than the administration of drugs or the act of surgery. One of the facts that seem to confirm this idea is that according to Eddy no more than 15% of medical treatments are founded on reliable scientific evidence. In addition, according to the World Health Organisation 280 pharmacological compounds can be used to cure 95% of all diseases, however, in Germany for example 6500 pharmacological compounds in 50.000 different medicines are in use of which 60% never have been tested for their effectiveness according to the governmental regulations inaugurated in 1978. It seems that many drugs “work” by other mechanisms than those called “scientifically” proven or effective and instead of ignoring the PE and treating it as a “negative

undesirable side effect", what a "scientifically" defined therapeutic effect really is and what it is composed of should be investigated.

Newly designed experiments based on mind interacting factors can be thought of. Patient test groups may for example be divided into "believers" and "non-believers", "frequent medical care experienced" and "occasional medical care experienced" or positive versus negative medical care experienced, receiving true or placebo drugs.

It may take long before no drug becomes the best drug for those many diseases, for which 60-90 % of surgical procedures and pharmaceuticals are of limited therapeutic use, and therapies are replaced by cheaper and sometimes more harmless alternatives. A process which has to be initiated and endured by physicians, as well as by patients themselves.

5.6 Literature

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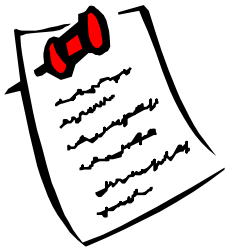


Conclusion

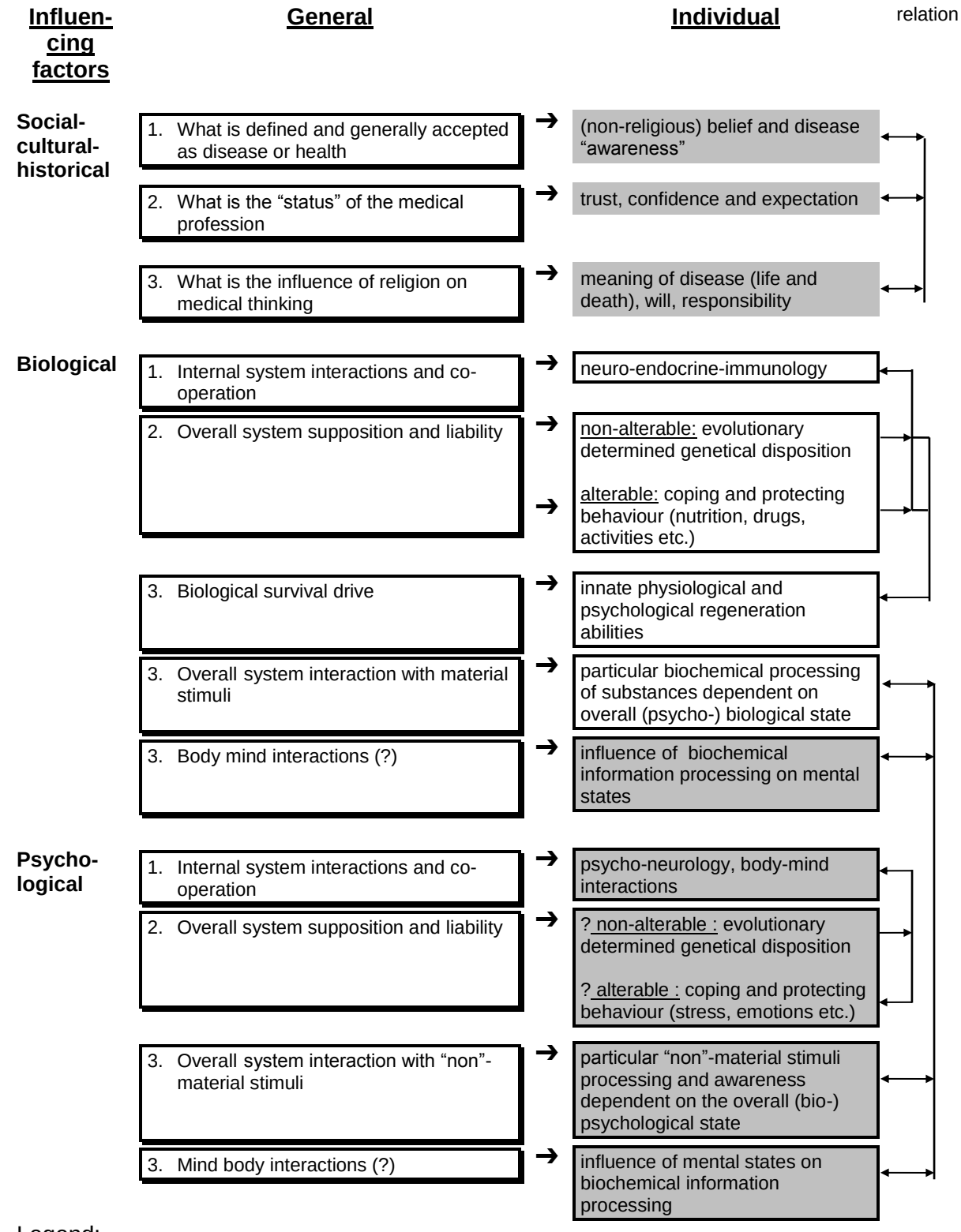
The previous five chapters described different world wide valid factors involved in disease and health. In spite of the enormous encouragement and achieved insights in reductionistic modern (biomedical) science, the single investigated and understood elements do not guarantee an explanation or prediction of the reactions of an individual organism as a whole. From the existing literature it becomes clear that some generalised concepts of distinctive biological working mechanism as investigated by modern biomedical-, biochemical- and molecular-gene research, not necessary can be expected to occur in the same way in the individual organism. A possible explanation for these findings can be searched for in the, up till now less well investigated, interfering physiological and psychological factors. Why a person stays healthy, gets ill, can be cured or not and which factors support these states seem to be much more complex than modern biomedicine has been able to answer so far. The less well examined and most unpredictable elements seem to be the “mental states”. Although some of them can be associated with physiological parameters, of most of them how and why they emerge the way they do and what their physiological effects or counterparts are, is still unclear. The world wide used different therapeutic methods, altogether achieving more or less cure but within each method often with non-consistent results, support assumptions that these therapies may more trigger internal healing processes than that they are the healing themselves. Mental states might be important components of these internal healing processes and future biomedical research trying to implement mental states may contribute to a better understanding of individual reactions on “standardised” medical treatments.

Although biomedical research has a high standard, claims to be highly reproducible and only announces the “truth”, its point of view is very fluctuating and new results strongly

depend on the used (new) technical methods. With all its knowledge, individuality and unforeseen occurrences which do not fit in are often ignored, however, in the end specially these events might be of greater importance for the comprehension of the overall observed reactions and results.

Table 7 is a summary of factors involved in health and disease. On the one side general elements are listed, on the other side what influence these generalised elements have on the individual. From this summary it becomes clear that many physiological (materialistic) processes, as they are examined by biomedicine, in addition may be influenced by mental processes. Without opposing biomedical research as it is done today, efforts should be made to better understand what mental states are and how they match in a materialistic orientated science. Part of the answers may come from neuro-consciousness research, but consciousness alone is not what mental states are. Another approach to better understand how people are cured is to search for similarities in all the available medical therapies. Not only by searching for the biochemical background of non-western or alternative medicine, but also by exploring what elements of these “alternatives” are implicated in modern biomedicine. Instead of the ethnocentric and limiting presumptions that take medicine *per se* as the object of study, healing and disease as universal events and empirical facts (sh)could provide the focus of research. Maybe answers on the many open questions which universally bother medical physicians and researchers should be searched for in a new theory on the interaction between body and mind. In the following part a hypothetical model of such an interaction will be introduced. Although absolutely theoretical and without the claim of being scientific in any form, such a thought construct may initiate new research approaches based on novel philosophical points of departure.

Table 7 Overview of factors influencing internal systems involved in health and disease

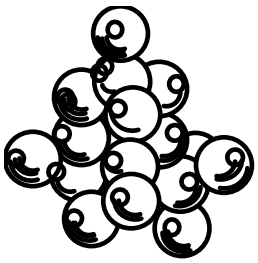


Legend:

= consciousness questions not included in biomedical research

= included in biomedical research

= hypothetical "ideal" combination of consciousness / biomedical research



Part two: a new theory

In the previous part it has been shown that health and disease are phenomena which cannot be reduced to material physical processes alone, but are as well under influence of the so called “mental” processes. Research implementing mental influences on health and disease is increasing but results are often inconsistent because mental states are difficult to 1)define, 2)measure, 3)describe objectively and 4)materialise. Medical research implementing mental influences partially limits itself on describing mental states and the observed physical influences without asking the underlying “how” these mental states are able to achieve such an influence. Consciousness research on the other side still concentrates only on what and how the brain is involved in consciousness, awareness and mental states without implementing the consequences their postulated hypothesis may have on the functioning of the rest of the body.

Independent from these unsolved questions is the fact that even in pure material biological research processes are described of which the question can be asked why they happen the way they do. The pleiotropic and redundant properties of many body own or artificial molecules arise the questions how such molecules know what to do or how to react the one way or the other.

The last few decades have been decades, in biology, of brain consciousness and genetic engineering, and technically of computation and information processing. Both directions have tried to involve each others knowledge in formulating and understanding the processes underlying “information transition and conversion”. In biology this has lead to a

shift of “a certain substance or process is information” to “a certain substance or process is the information carrier”. Pleiotropy and redundancy of substances or processes may be explained in terms of the information they carry and not by the information they are. However, because of a lacking universal definition of information, where information itself is produced or what it is “made” of remains unclear.

In the following chapters it will be tried to develop a concept of biological information processing which may help to understand the interaction between physiological processes and mental phenomena as described in part one. First, in chapter 6 some pleiotropic and redundant phenomena of body substances will be described to illustrate the issue. Chapter 7 will cover aspects of physics with a similar problematic concerning information processing and serve as a model and guide for the concept. The concept itself will be introduced in chapter 8, followed by chapter 9, covering the implications the concept has on medicine. The last chapter 10 will deal with the possibility to investigate and search for proof of the concept.

6. The shunned unasked questions

6.1 Introduction

The 20th century has been the era of the resolution of the biochemical mechanisms underlying life. Research more and more looked at smaller units from organs to cells and from cells to organelles and at last molecules. Production, function and mechanisms of actions of hormones, neuropeptides, neurotransmitters, genes etc. now have been resolved and described in terms of (bio-)chemical interactions of molecules. The biochemical research did not restrict itself to body functions but also implemented biochemistry involved in behaviour and mental states. Hundreds of substances have been discovered and characterised so far, however, the initial categorisation into functional groups such as “hormones”, “neurotransmitter” or “interleukines” soon had to be revised as many substances showed multi-functionality. On the other side special functions seemed not only restricted to one substance but could be executed by others sometimes as “simple” as ions.

Exploring the biochemical mechanisms behind certain life functions such as the metabolic pathways, cell replication, protein production etc. have shown that these processes are immensely complex and regulated, influenced and completed by many substances. Although some of the involved substances have been described by now, how the production of the involved regulating substances themselves is regulated is mostly unclear.

The wish of modern science to understand the world in terms of simple universal equations valid for all physical and biological processes has led to the introduction of a new terminology in biology. Hormones, neuropeptides and others now are seen as messengers carrying information and receptors for these substances as the place where information conversion takes place. In the following some examples of biochemical processes will be given which show that the introduction of “information” as such seems to be necessary to understand how biochemical substances can accomplish their function(s).

6.2 Pleiotropy

Pleiotropy comes from the Greek language and means the simultaneously occurring characteristics of a substance, according to that the substance can be assigned to a complete radius of actions. Some simple kind of pleiotropic characteristics of a substance can be seen all over chemistry because most substances can react with many others (in comparison the word “bank” has at least two different meanings and can be combined with “to sit on” or “to get money from”) More problematic is the question which interaction

will occur when in a certain situation two or more reactions are possible (“do you see the bank over there ?”). Only with additional information a decision can be made what the aim of a certain interaction is. In chemistry this information may come from the concentration of the interacting substances, the strength of the reaction and the achieved equilibrium, however, as will be revealed below sometimes parallel processes using a single substance to obtain different reactions may be at work.

Another form of pleiotropy can be observed when similar physiological processes result in different mental states. Stimulating a sense organ (like tickling) may result in a pleasant or unpleasant feeling although the primary physiological processing of the stimulus in both cases is the same. Again additional information to the stimulus seems to influence the decision what is going to be felt.

6.2.1 Hormones and neuropeptides

Hormones and neuropeptides are a good example to show pleiotropic characteristics. Not only has one hormone many different effects but also, for some substances, the border between hormone or neuropeptide or even neurotransmitter is unclear. Classically, endocrine hormones are considered to act at sites distant from their tissue of origin (endocrine function), however, this idea has been revised as for many hormones it is now known that they also react to cells close to those who secrete them (paracrine function) or directly on the cells of origin (autocrine function). Hormones and neuropeptides are not directly involved in the reactions they want to regulate but only serve as informants that a certain reaction should be initiated or stopped. In the following the multi-functionality of some hormone/neuropeptides will be listed.

- adrenaline *hormone/neurotransmitter*
  glycogen breakdown
  increases lipolysis
  increases heart rate
  contraction of vascular smooth muscle
  decreases T-cell reactivity
  increases NK cell activity

- insulin *hormone*
  glucose metabolism (cell glucose uptake)
  decreases lipolysis
  growth stimulation
  modulates DNA transcription
- oxytocin *hormone*
  promotion of uterine contractility (to expel the fetus from the female tract)
  facilitates the scent of spermatozoa in the female tract
  increases nursing behaviour
  induces lactation
- substance P *neuropeptide*/*neurotransmitter*
  excites intestine activity
  decreases blood pressure
  involved in the pain pathway
  involved in infections
  stimulates antibody secretion and lymphocyte proliferation

The above mentioned hormones/neuropeptides/neurotransmitters all show a widespread functionality. Whereas specific modes of actions can be explained in that only certain cells express receptors for a hormone, more generalised modes of action (like substance P stimulates antibody production by, and proliferation of lymphocytes) cannot be explained by specific receptors alone. Similar lists can be made for neurotransmitters which are involved in different kinds of behaviour or mental states or neuropeptides influencing brain activity.

In addition to the numerous functions one hormone can have, the signal transducting pathway initiated by the hormone itself can be pleiotropic as described in the following.

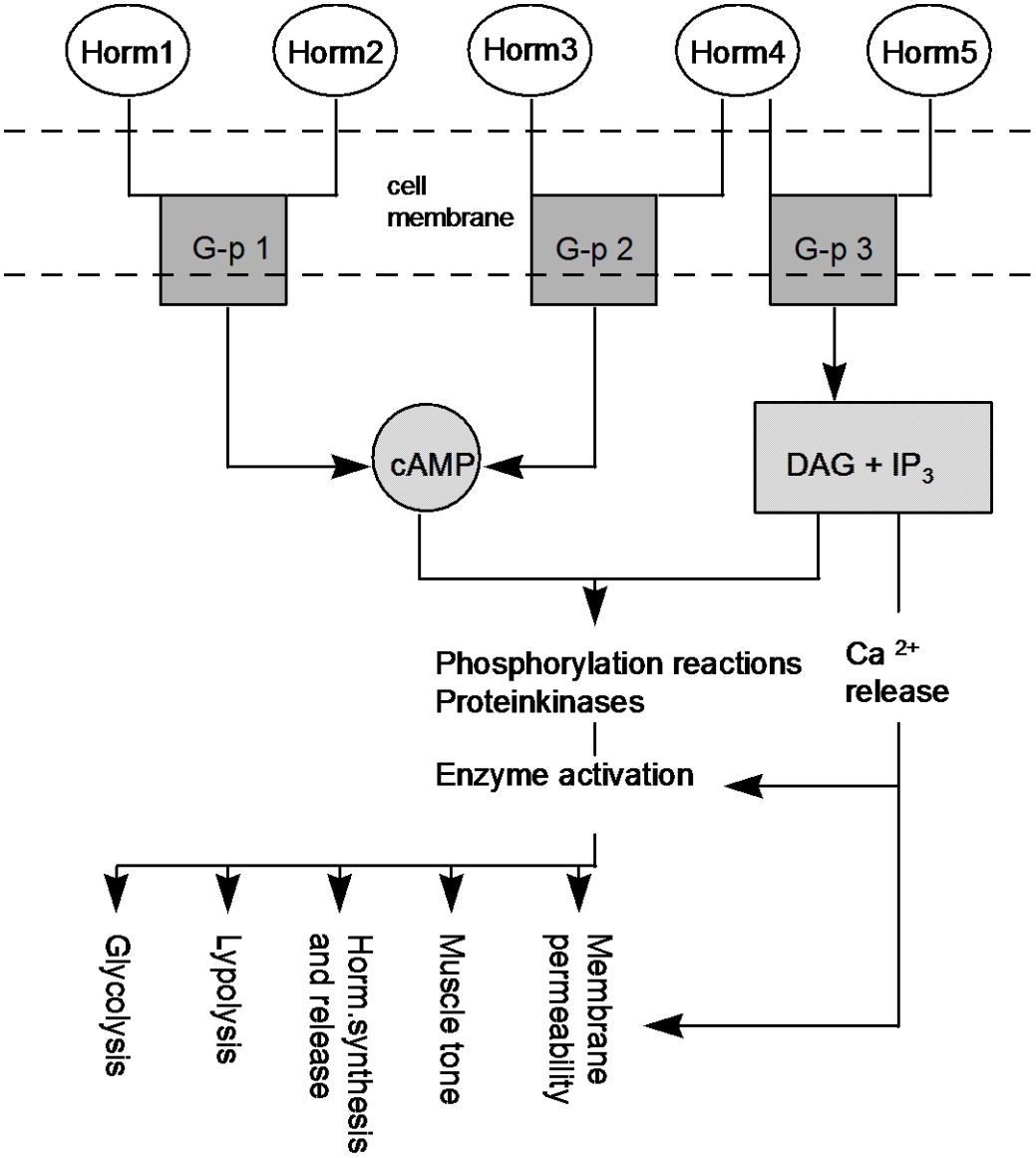
6.2.2 Second messengers

Peptide hormones, neuropeptides and neurotransmitters in general do not enter the cell but bind to specific receptors on the outside of the cell membrane, initiating a cascade of reactions which generate the appropriate metabolic response. The hormone (neuropeptide or neurotransmitter)-receptor complex binds to a series of so called membrane-localised G-proteins of which at least 3 types have been found. The activated G-protein complex then exchanges a bound GDP (guanosin-di-phosphate) molecule with a GTP (guanosin-tri-phosphate) molecule and thereafter can

1. bind and activate the enzyme adenylcyclase which produces cAMP (3'-5'-cyclic-adenosin-mono-phosphate) out of AMP
2. bind and activate the enzyme phospholypase C-γ which produces inositoltriphosphate (IP_3) and 1,2-diacylglycerole (DAG) out of phosphatidylinositol biphosphate

cAMP in turn mostly causes an activation of regulatory proteinkinases which modulate enzymes within the cell by phosphorylating serine or threonine, or it can change cell membrane permeability. IP_3 on the other side binds to sites on the endoplasmic reticulum, opening Ca^{2+} channels and allows stored Ca^{2+} to flood the cytosol. There it modulates numerous enzymes, many by activating their calmodulin or calmodulin-like subunits. DAG has two functions: it activates proteinkinases and opens Ca^{2+} channels in the cell membrane. The different kind of G-protein complexes exhibit stimulatory or inhibitory properties which are both transmitted by cAMP. A schematic presentation of the hormone actions is given in Figure 6–1 and shows clearly the "bottleneck" towards the so called second messengers cAMP, DAG, IP_3 or Ca^{2+} and from those second messengers to all kind of cell processes.

Figure 6–1 **Hormones second messengers**



Although the system has a high specificity at the hormone receptor side, inside the cell this specificity seems to get lost. Cells mostly express receptors for many different hormones or neuropeptides regulating diverse cell functions using the same second messenger (for example thyrotropin, adrenaline and ACTH on B- and T-lymphocytes, the first stimulating antibody production, the second inhibiting T-cell reactivity, the latter stimulating or inhibiting antibody production and inhibiting γ-IFN production by T-cells all by the second messenger cAMP). The question arising from this hormone-second messenger system, when a cell possesses more than one hormone receptor using the same second messenger, is how cAMP, DAG, IP_3 or Ca^{2+} know by which hormone or neuropeptide they were stimulated and which specific enzymes have to be activated or inhibited.

6.2.3 Steroid hormones

Steroid hormones encounter similar difficulties as peptide hormones where they have to transmit information. Steroid hormones in contrast to peptide hormones do enter the cell where they bind to a cell plasma receptor. The hormone-receptor complex then enters the nucleus where it combines with the chromatin and is closely associated with (or even binds to) DNA and initiates genetic transcription as a result of an increased action of RNA polymerase. Messenger RNA and the belonging proteins then are synthesised and in turn initiate the hormone's effect. The effect a steroid hormone can have may be very diverse and the question arises how the activated RNA polymerase knows which DNA (=gene) has to be transcribed. Testosterone for example is responsible for spermatogenesis as well as it has anabolic actions (promotion of protein anabolism). From entering the cell up to its binding in the nucleus and activating RNA polymerase in all cell types bearing testosterone receptors the same seems to happen, than however, depending on the cell type other genes are transcribed and the end effect is totally different.

6.2.4 Drugs

Not only biological organism own substances do have pleiotropic characteristics, also (pharmacological) non-biological chemical substances exhibit this characteristic when they enter an organism. In medical terms the pleiotropy of a pharmacological substance is called "side effect". Reading the patient's information of a medicine illustrates the subject: for instance the medicine Voltaren® [5] contains the active substance diclofenac-potassium which has a strong analgesic and inflammation inhibitory action. However, it can for example also cause heartburn and pain in the stomach, tiredness and general feelings of indisposition, nausea and vomiting with loss of appetite, vomiting blood, blood in the urine, skin irritations and itchiness, short breath, yellow colouring of skin and eyes, sore throat or fever, swollen face feet or legs, headache, breast pain and coughing. The list of possible side effects is at least twice as long as described above and although these side effects do not have to occur at all, the question can be asked why they sometimes do.

Even if diverse drug effects may be caused by concentration variations and/or different chemical interactions a substance can be involved in, it is unclear from a material point of view why they not all, not always and in the same as well as in different individuals can be observed or not. Beside the chemical interactions and reactions a drug may execute in the

[5] From the patients information of Voltaren®Rapid, Diclofenac-Potassium 50mg, CIBA-GEIGY AG, Basel (1995)

body, some other unknown factor(s) seems to play a role in how far those reactions in the end will take place.

6.3 Redundancy

Redundancy comes from the Latin word redundantia and originally means superabundance or superfluous. The biological meaning of the word is that more then one substance is able to achieve, activate or cause a certain reaction to realise a particular goal. Different substances may realise the goal by activating the same pathway or by activating different pathways. One of the reasons evolution may have “introduced” redundancy is to provide an organism with more than one system for the same goal, so that if one system gets damaged another may take over. Another reason redundancy exists is that different higher goals need the same underlying lower goals for their realisation (see 6.3.1). The pharmaceutical industry uses redundancy to produce ever new and more medical drugs to cure a same disease. In the following some examples will be given to elucidate this phenomenon.

6.3.1 Hormones and neuropeptides

As already shown in chapter 6.2.1 one hormone may have many diverse functions. However, this is also true the other way around: one function may be regulated by different hormones/neuropeptides. For example blood glucose levels can be elevated by glucagon, adrenaline, corticosteroids and growth hormone. Whereas glucagon, growth hormone and adrenaline use the same signalling pathway by the second messenger cAMP, corticosteroids are steroid hormones and use a complete different signalling pathway to reach increased blood glucose levels. Although the first goal: to elevate blood glucose levels and make energy available, can be executed by these four hormones, all of them are activated to serve another purpose (glucagon to set free energy for all kind of body activities, adrenaline to set free energy for a flight or fight reaction, corticosteroids to set free energy in stress situations and growth hormone to set free energy for growth and body cell maintenance). Beside blood glucose elevating properties the same four hormones increase blood fatty acids. Both glucose and fatty acid elevation serve the higher goals of the hormone (all to set free energy for a certain purpose). The opposite of setting free energy is to store energy in form of glycogen for example in the liver which is stimulated by insulin. Both glucagon and adrenaline decrease glycogen levels in the liver but corticosteroids don’t, instead they elevate glycogen levels in the liver.

Table 8 **Effects of different hormones on blood glucose, blood fatty acids and liver glycogen levels**

Hormone	Blood		Liver
	Glucose	Fatty Acids	Glycogen
Insulin	↓	↓	↑
Glucagon	↑	↑	↓
Adrenaline	↑	↑	↓
Corticosterois	↑	↑	↑
Growth hormone	↑	↑	-

Legend: ↓ = decreased levels, ↑ = increased levels

Many other examples may be found in the living organism showing redundant properties of substances or processes.

6.3.2 Drugs and treatments

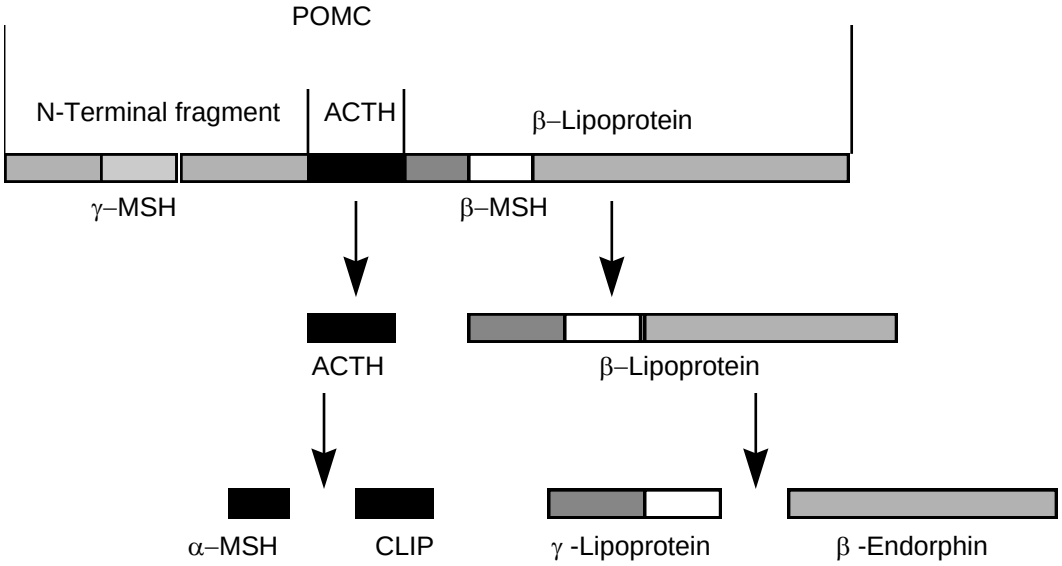
Not only biological organic substances show redundancy. Chemical artificial manufacture substances with different chemical properties may serve the same goal. Pain inhibitors are a good example. Acetylsalicylic acid (Aspirin®) or ibuprofen (Solufen®) both inhibit prostaglandin production, or acetaminophen (Panadol®), mefenamine acid (Ponstan®) or tramadolhydrochloride (Tramal®) with less known mechanisms of action, all are analgesic drugs, but all have a different chemical structure. Even the application of other treatments then drugs like massage, acupuncture or meditation may decrease or inhibit pain. In contrast to the example of hormones, where an identical effect (glucose level elevation) serves, in the end, different goals, these drugs and treatments have (almost) all a different (chemical) effect serving the same goal.

Although the complex pain system allows several points of interference, not all individuals react the same on each treatment or one individual always the same on one certain treatment even though the “material situation” in these circumstances seems identical.

6.4 Post-transcription protein modulation

Molecular biological investigations have shown that many proteins are not one to one linear identical with their DNA sequence. Somatic modulations such as RNA splicing, self-catalysed protein splicing and/or enzymatically protein splitting determine what active end product is produced. In the following one example of enzymatically precursor proteins splitting will be given. The protein proopiomelanocortin (POMC) is produced by cells of the hypophysis or the immune system and its production is controlled by CRH. The POMC protein contains the active proteins ACTH, β- and γ-lipoprotein, β-endorphin, α-,β- and γ-MSH (melanocyte stimulating hormone).

Figure 6–2 **The POMC precursor protein and its products**



In contrast to RNA or protein splicing where the splicing junction seems to be determined by the nucleic acid base sequences or the amino acid sequences and their chemical characteristics, enzymatic modulation of precursor proteins are based on enzymes who know where to cut. Consequently, in the case of POMC, to get for example ACTH and not CLIP + α-MSH, CHR must not only stimulate the production of POMC, but somehow the regulation of the enzymes knowing where to cut what, to obtain this ACTH also must be organised.

6.5 Comments

Reduction of life systems to (bio)chemical reactions gives rise to some interesting problems. First chemical reactions happen according to the physical properties and the concentrations of the reacting substances. If the conditions permit a reaction between two substances this reaction just seem to happen spontaneously. According to physics and chemistry reactions themselves have no aim but happen because they are driven by their physical characteristics and according to the laws of thermodynamics. In biology however all reactions seem to fulfil a certain purpose and the language biologists use is one of “cause”, “goal”, “meaning”, etc. Reactions are not thought to happen just by coincidence because substances incidentally meet each other but always because they serve a certain process and are actively and well directed “brought together”.

The reaction of two substances mostly results in a third (new) substance with own physical and chemical characteristics and in biology a new “meaning”, however, whereas

the physical and chemical characteristics of such a substance are substance bound, a certain “meaning” may be shared by different substances (redundancy) or one substance may contain and transmit several “meanings” (pleiotropy).

Research on the molecular level has revealed that the material properties of (reacting) substances themselves are not sufficient to explain what does happen in a living system, like DNA does not contain the key to its own interpretation. The introduction of communicational terms in biochemistry such as “goal”, “signalling”, “messenger” or “information carrier” to explain reactions have nothing to do with the physical properties of the substances and assume that something has to be put into context and interpreted in order to work. Similar to the problem of the “homunculus” in the brain interpreting consciousness, the body seems to need its homunculus not only to interpret but also to decide and order for biochemical processes.

Although matter-matter interactions seem to make up what is called “living organisms”, these interactions not only produce new or other substances but also seem to produce some kind of information, information which is interpreted (information-information interaction) and influencing matter-matter interactions. In the following chapter a closer look at physics and its view on information will be given in order to explore what biological information, its existence, processing and transmission, might mean.

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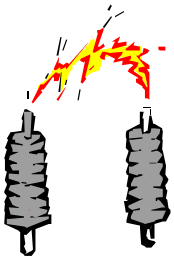

7. A look at physics

7.1 Introduction

Living organisms are macro-phenomena consisting of micro-elements. Physics is a science which tries to describe and understand the micro-elements and formulate uniform laws describing their behaviour and interactions. To understand the processes in living organisms it is believed that the physical laws of elementary micro-elements in the end will (help to) explain life processes, including consciousness. For example Searle, in "The rediscovery of the mind", formulates these expectations as follows: "…one can accept the obvious facts of physics - that the world consists entirely of physical particles in fields of forces-……essential to the explanatory apparatus of an atomic theory is not only the idea that big systems are made up of little systems, but that many features of the big ones can be *causally explained* by the behaviour of the little ones…". In relation to the questions asked in chapter 6 and the phenomena described in part 1, physics in the end is expected to explain for example how the elementary micro- elements of a certain substance (like cAMP) can induce different effects, not only how they do so but also why they do so and why at different moments the one way or the other.

Physics, as the science of elementary matter and forces, is hoped for to verify a monistic material life view in favour of the modern biomedicine so that life itself can be predicted, understood and manipulated by physical/material laws. In the following a closer look at certain components of the physical knowledge gained so far will be given, however, only some results will be described, without going into the details of the experiments and explanations. The described observations are only meant to show the problematic physics itself is dealing with and lighten why reducing biological phenomena to physical phenomena might or might not increase the understanding of life phenomena.

7.2 Physical pluralism

Whereas life in the modern world is thought to be "material" and therefore a monistic phenomenon (including the "mental") physics reveals that what makes up macro-elements (molecules/matter) when reduced to micro-elements (elementary particles) is not at all only "matter". Physics itself is dualistic, pluralistic or even mystic.

➜ Characteristic dualism

Characteristic dualism means that one substance may have different characteristics like elementary particles may appear as matter or as wave depending on how they are observed. Particles like photons or electrons can be measured in experiments as a wave or as particles but never both at the same time. For such particles it is described that "they

know and/or *decide* whether they will come out of the experiment as a particle or as a wave". Essential to the characteristic dualism is the observation. Only by observing (putting elementary particles in an experiment) the one or the other characteristic will be observed and therefore this kind of dualism might be an illusion in so far that only a characteristic is measured which was asked for. Asking other questions with other experimental settings might reveal other characteristics not known so far.

➜ Pluralism

Not only can particles behave according to their "will" as wave or particle, they also seem to contain matter, energy or force. Containing mass implies containing energy according to the law $E_{(nergy)}=M_{(ass)}C_{(light\ velocity)^2}$ but also particles with no mass but with energy seem to exist. Moreover as soon as more then one particles come together they exhibit forces like gravitation or electrical forces. Moving particles in addition may induce fields like when electrons move through a wire an electromagnetic field occurs. Fields and forces do influence the behaviour of other particles and the own particles causing their existence, "telling" them how to behave. This substance - substance interaction may function between the same kind of particles (photon-photon interaction) as well as between different types of particles (photon - electron) interaction.

➜ Mysticism

Something out of nothing:

Although it is generally accepted that the total energy/mass of the universe is constant, a situation may be observed where something (particles) appears out of nothing. For example a total vacuum is thought to contain nothing, still in a vacuum photons may appear for a short while "borrowing" the energy from the vacuum. Such photons may be detected, thereby giving their energy away to the detecting system instead of back to the vacuum.

Uncertainty principle:

Particles are always in motion as long as the temperature has not reached the absolute zero. The scientist Heisenberg has found out that one cannot determine at the same time the exact position and the exact speed of a particle. The more exact one knows its position the less exact one knows its speed. The consequences of the Heisenberg uncertainty principle are that no absolute deterministic model of the universe including living organisms can be given. Measuring one characteristic of a system decreases the exact determination of a related other characteristic.

Undetectable particles:

The forces between matter like gravitation or electric forces seem to be caused by particles with force. They are emitted by a matter particle and absorbed by another matter particle thereby changing the behaviour like speed of both matter particles which gives the impression that a force is working on them. These force particles are “virtual” because they cannot be detected and never have been “seen”, but their existence is believed in because they are supposed to be responsible for the measured forces between “real” particles.

The most important answer physics seem to give is that it has shown that the experimental observation of a certain situation lets the situation “collapse” in a certain state thereby destroying what was observed. Certainties can only be obtained by collapsing the uncertainty and that the observer decides which certainty will be seen. Asking different questions will give different answers and although all answers may be true for their specific experimental setting, the pluralistic view they bring about shows that even at the level of micro-elements nothing seems to be very clear and predictable. Moreover, as for macro-elements (molecules) micro-elements are thought to be able to do more than only be there. They have a “behaviour” and “locate” all possible routes of an experiment (probability waves) before they “decide” to be in one state or the other, they can react on a force or field if they are able to “receive” the proper information of that field. They seem to have a genotype and a phenotype, whereby the phenotype first appears under influence of the environment. Although physical laws seem to describe the behaviour of micro-elements quite well, as for macro-elements, it may be questioned whether this description is an explanation of how they know how to behave.

7.3 Information

7.3.1 Information as an elementary physical component

In addition to the science of elementary particles, from the 20th century on physics has paid more and more attention to “information”. The universe not only contains particles with or without mass, force or energy but these particles in interaction somehow seem to carry and transfer information. The first definition of information was given by Shannon and Weaver and says that information is a mass for fortuitousness and can be measured in the unit “bit”. To illustrate this definition the sequence AAAAAAA has a much less informational content (it can be reduced to 7xA and therefore has not much fortuitousness) then the sequence ABBAAAB (which can be reduced to 1A followed by 2B, 3xA, 1B or 1xAB, 1xBA, 1xAA and 1 B etc.). Whereas in theoretical physics,

mathematics or programming languages for computers information itself is a “described” element measured in bits, in (the living) nature it is completely unclear what exactly information is. There are several speculative possibilities to define (natural) information:

1. Information is an elementary part of the genotype of particles like mass, energy and force and becomes apparent as soon as particles interact. Like for forces it can be postulated that the carriers of information are undetectable virtual particles which are transposed between the “real” particles.
2. Information is an emergent phenomenon upon interacting particles: the creation of new properties at a certain level of organisation which cannot be predicted from the properties found at lower levels.
3. Information is a “by” or “side” product of interacting particles like heat.

The main question in the above postulated definitions is whether information exists as an elementary property or not and whether it as such can be detected or only its repercussion. Does information underlie the laws of physics and can its appearance and its content be predicted from the characteristics of the particles it seems to originate from ? Furthermore it is unclear whether information can influence the behaviour of particles like field forces do or not. The pluralism of matter-energy and forces maybe should be implemented with information, where matter-energy-matter interaction “cause” the information force field as well as this information may act on matter-energy-matter interaction like a force field.

7.3.2 Information and entropy

Another physical point of view interprets information having the same kind of character as entropy: macro-states which can be realised by many different micro-states, with more disorder, have a higher entropy or informational content as such macro-states which can be described by a few micro-states, with less disorder. With increasing disorder and complexity of a system the amount of information increases, however this is not information which is available. In daily life useful information about a system or macro-state is how much of the information of the micro-states is not essential or can be drawn out to describe the macro-state. Not the available (micro) information is essential but that part of the information which can be left out. This idea as described by Nørretranders (see…) can be illustrated as follows: by writing down the words as done in this script huge amounts of information as processed in the mind of the writer has to be omitted in order to become a reasonable amount of information. If the reader could only obtain the information by knowing all the processes going on in the brain of the writer (up to the smallest element) books would never have been written. The words as they are written

down somehow implement all the information which has been left out by the writer. Its up to the reader to enlist this excluded information, which is (as hoped for) automatically done by the brain of the reader when he/she reads the words, although the writer never will be sure that the reader includes the same information as was excluded by him/her during the writing. The idea of subtracting information to get information may play an important role in biology, like it is almost ambiguous that the mere DNA code given by the sequence of 4 bases can account for all aspects of live. It may not be the code itself but what has been left out during the creation of the code, when by reading/translating the code is implemented again, what makes up the real informational content of DNA.

In nature micro-systems aspire for higher entropy = disorder = lowest energy + high informational state. Entropy is worked against by the attempt of macro-systems for enthalpy = order = higher energy + lower informational state. The reduction of macro-systems to their micro-system will supply scientists with more information, but it is unclear whether this increased information amount will bring more understanding because what can be left out might be of more importance and meaning.

7.4 Physical-biological analogies

Exploring micro-systems or elements in order to find answers about macro-systems may be helpful in another manner than that of explaining the one causally by the other. As described in chapter 7.2 the behaviour of micro-elements can be described by the laws of physics, however these laws do not really explain the “why” (why do matter particles transpose “gravitons” to produce gravitation) but more the “what” (matter particles have to transpose gravitons otherwise gravitation cannot be explained). Finding analogies between micro- and macro-systems may lead to a better understanding or at least acceptance of certain phenomena than trying to explain these phenomena as causal effects.

The most fundamental phenomenon throughout the description of micro-and macro-systems, from physics, chemistry, biology to psychology and sociology, is that of emergence. At least three types of emergence valuable for micro-and macro-systems can be observed which will be outlined in the following

➜ Interaction emergence

With interaction emergence is meant that as soon as more then one element come “together” a “need” to interact emerges, creating qualities between the interacting elements which can not be observed for the single element. The necessity for this “need” is unclear as one might imagine this “being together” without the appearing emergent qualities. Some examples for this type of emergence are listed below:

- One electron alone has no real charge, only when electrons meet other electrons or positrons they have a charge and distract or attract each other
- One atom or molecule alone has no pressure, only when many atoms or molecules come together they can have pressure
- One molecule H_2O is not fluid, only many molecules H_2O make water fluid
- One nerve cell alone may not have consciousness, many together do have
- One organism alone will not have communication or develop language, many together do communicate and can develop language

This list may be continued infinitely, from the smallest elementary particle to the most complex system or process.

➜ Motion emergence

Motion emergence describes those phenomena which appear when elements come into motion thereby causing effects which they do not have in standstill and which are not characteristics of the elements themselves. Some of these emergent phenomena can be detected by the sense organs of organisms, others may exist of which humans have no notion of at all because they are not able to detect these characteristics themselves or indirectly by measuring instruments transforming these characteristics into detectable ones. The following examples clarify motion emergence:

- moving electrons in a wire give rise to an electromagnetic field
- moving air (in waves) gives sound
- moving photons give light
- moving molecules or atoms give temperature
- moving depolarisations along a nerve cell give information (and consciousness ?)

Again one might imagine all these moving elements without producing their emergent characteristics and they only seem to exist for those who are able to detect them, still they would not be there when the movement would be stopped.

➜ Fusion emergence

One of the best-known examples of emergence is that of “the product of two elements is not a mere sum of the separate elements”, like the chemical combination of two substances, each possessing a number of specific and known properties, creates a new substance with properties which could not be predicted from the fusing substances. This kind of emergence again can be found throughout nature from the smallest elementary particles to the biggest macromolecules including characteristics such as solubility, reactivity, form, collar, taste etc.

What all types of emergence have in common is that they have a kind of subjectivity. The emerging characteristic requires a perceiving subject being able to perceive or construct the patterns involved. This might be mostly true for information, in as far as information can be considered as an emergent characteristic (depending on what is meant by information all three kinds of emergence as described above might have information as a new property).

7.5 Comment

The (emergent) need of humans to explain life including themselves has lead to the paradox phenomenon of thinking out laws which try to explain that what has thought them out in the first place, or in other words does physics as a product of our thinking can explain our thinking ? What physics can learn other sciences is that somehow everything is relative to the context it is placed in and that pure determinism does not seem possible. That more information not necessary leads to more understanding and that describing phenomenons and predicting their behaviour does not mean they are explained. In general it can be questioned what is meant by explaining. Digging deeper from macro to micro alone does not explain but only increases the amount of information, in addition emergent phenomena, so far, are out of the reach of explanation, they just exist. Of many (biological) processes a description and laws can be given but these still do not explain why they happen in the first place. With the introduction of the term “information” even more confusion turns up, mainly because of the many existing different definitions. That the expression “information” is hard to handle specially in respect to biology will be discussed in the following chapter.

7.6 Literature

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8. Biological information processing

8.1 Biological information

In biology the definition of what information is, is very difficult. According to the mathematical and physical theories of information, information is an objective existing measurable entity. The translation of this theory to biology results in the idea of objectively existing properties of so-called informational molecules such as DNA and RNA or proteins, resulting in the famous “central dogma” formulated by Francis Crick that information can be passed from DNA to RNA to protein but never the other way around. Information, then, is a “thing” and something which can be moved or transported. The problem about this conception of biological information is that while information as understood by physicists has no connection to values, relevance or purpose, biologists think about information as always serving a purpose in the system. In addition DNA does not contain the key to its own interpretation and is dependent on proteins (giving information) to start its informational transfer.

Biological information therefore is inseparable from its context and has to be interpreted in order to work. This insight has forced some scientists to define information as only to exist as long as it can be detected (or even when it gets into consciousness). However, humans have developed technologies which make it possible to (indirectly) detect information they themselves cannot receive by their sense organs, by transforming the information into a form detectable for their sense organs. This has made the discussion on what information is more difficult. Does information play only a role when it can be made conscious or can information be implemented in processes which are not conscious? Furthermore information thus can be transformed from one form to another in order to be received. Summarising it can be formulated that biological information itself is only a part of the problem. First it must be questioned where it resides, secondary how it is transmitted (and eventually transformed) and in what form or on what carrier, third how it is received and forth how the receiver interprets it’s content.

Whereas the first two items are still unsolved for the third and fourth item some ideas have been postulated. The most accepted concept of receiving and interpreting information is that of the ability to distinct between differences. Yet this concept generates the problem of at which point in pre-biotic (starting with elementary particles) systems the ability of turning differences in surroundings into distinctions appear, or in other words at which point does a system acquire self-reference.

Without being able to solve all the problems concerning information, in the following section speculations will be introduced formulating a new concept on biological

information. The aim of such a speculative “thought play” is to present a different entry into the material world view as believed in by modern (biomedical) science.

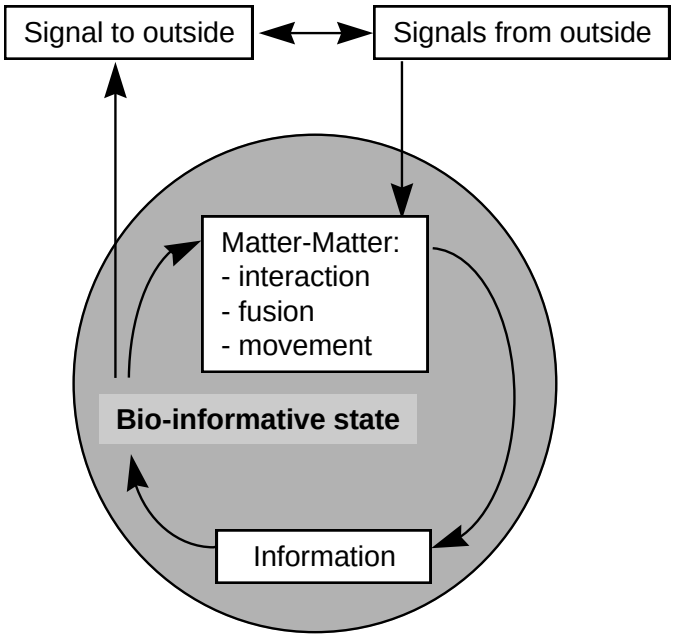
8.2 Bio-informative-state

Assume that information is a genotypic property of the elements nature consists of, which appears as an emergent property of the interaction, movement and/or fusion of matter/energy and has the characteristic of a force field. The implication of such an assumption for living beings is that out of all on-going processes in the organism information emerges (from the smallest units up to the most complex units) which influences (at the material/energetic level) the behaviour and reactions of those ongoing processes (in analogy for example that electrons are influenced by electromagnetic fields but themselves can be responsible for or causing the electromagnetic field). So all internal biochemical reactions and those initiated by incoming external signals contribute as an emergent property to a “informational field” in an organism which can be “received” by all contributing processes of interacting, fusing or moving matter/energy (see Figure 8–1) which will be called the “bio-informative state” (BIS) of an organism. A definition of the BIS can be formulated as follows:

The bio-informative state of an organism is the sum of all emerging information out of all on-going biochemical processes in an organism and has the characteristic and property of a force field.

A biochemical material process, then, is not only defined by the physical properties of the interacting substances but also by the available “surrounding” information interfering with the biochemical reaction.

Figure 8–1 **The bio-informative state**



Although this model looks much like a feedback system, for the BIS it is thought that information not only interacts with the elements responsible for its emergence, but also is available for and may interfere with unrelated processes. The BIS, as a field, is everywhere in the organism (and maybe even outside?) thereby connecting and “informing” processes which are not directly (material) linked. Taking into account that a postulated BIS does not at all solve and explain the problem of emitting, transmitting and/or transforming, receiving and interpreting information, the model provides a hypothesis that information is an elementary efficacious and maybe even the key ingredient of life science. What consequences such a hypothesis may have on the understanding of biological processes and medicine will be discussed below.

8.3 The body and information processing

From the simplest, smallest living organisms (including viruses and priones) to the most complex ones, an incessant interaction (in)between the organism and its environment is going on. To be able to survive and reproduce any organism must know what is going on outside and inside itself. The more complex an organism gets the more information it needs to collect to become the necessary in- and outside knowledge for its functioning. What is outside mostly is not available in a representative form for the inside, therefore the outside is taken inside by the help of transforming its information in a “understandable” manner for the inside. In complex (higher) organisms part of this transformation of

information takes place at the sense organs, transmitting the information by the central nervous system to the brain. As far as known by now, this information translation and transmission itself is thought to be a material process. All the actions, interactions, movement and fusion of matter during this information processing contributes to the BIS, thereby making the information available for the whole system. A similar sequence can be described when a pathogen enters an organism and the immune system comes into action.

Essential to the assumption of a BIS is that the first contact and translation of outside information (light, sound, taste, pressure, smell, pathogens), as well as system intern information, with and into the material processes of an organism occurs within the BIS environment and may be influenced by it as well as this contact and translation changes the content of the BIS itself. Now one may ask why the material components of a system are not enough to explain biological processes. As already described in chapter 6 and part 1 of many possible ongoing processes or biochemical reactions, beside the merely physical properties, a kind of “knowledge” is required. Reactions which can occur not always do (like the intake of a drug not always has an effect although the chemical premise is given) or substances which are involved in different processes must know which process they have to initiate (like cAMP) and even reactions may occur where there does not seem to be a material equivalent (placebo). The BIS could be one of the sources for this knowledge. Furthermore internal information exchange between different systems like the immune and nervous system until now only partially can be explained by their material components. So the BIS may play a substantial crucial role on biochemical processes.

8.4 The bio-informative state and consciousness

So far it has only been talked about the BIS and biochemical (unconscious) body processes. At least for sure in humans, parts of the information processing leads to consciousness whereby it is unclear why and how certain information becomes conscious and other doesn’t. Now it may be speculated that consciousness is an emergent property of the BIS: summarising all the available information leads to the new property consciousness. Conversely only very little of what is happening in the body becomes conscious. Somehow much information has to be omitted before it becomes conscious which does not mean that this excluded information is lost and unimportant. The difficulties biomedical and PNI research have with implementing the mental states and consciousness in their material orientated investigations is that of not being able to imagine the influencing connection between mind and matter. What the consideration of

consciousness being a part or some kind of emergent property of the BIS can propose is that consciousness, besides being a product of material processes, may have influence on these material processes (as far as information is assumed to be a physical entity as suggested in chapter 7.3). Without creating substance dualism as done by Descartes, information is part of the character pluralism of matter, with consciousness as one of the possible realisation forms. Although it is clear that such a theory does not answer why "we feel the things we do" it may contribute to the understanding of how, as often observed, mental states and consciousness influence body processes, without conflicting the physical laws.

Another point of view concerning the BIS and consciousness can be that the BIS represents the "self" and consciousness the "I". The sentence "Deep inside I know that … but I can't put it into words" may represent the BIS, knowledge/information the conscious "I" not always wants to know about, be aware of or trust. Furthermore, mental states such as belief and confidence, which only seem partially accessible for consciousness, may "reside" in the BIS.

8.5 Comment

First of all again it has to be emphasised that all what has been written above is purely speculative. The idea behind the speculation is to connect scientific findings of different disciplines, until now thought as being true, and extrapolating them into a system overlapping hypothesis in order to find answers implementing reductionistic and holistic thoughts. Aside, this speculation has to be seen in the context of the contemporary issues of interest: no thought about "information" would have come into mind in an"information absent society". The hypothesis of the BIS is no more than one out of many, trying to describe (not explain), as hoped for more or less scientifically, certain phenomena not being fully understood by pure physical or biochemical laws so far.

If such a "thing" as the BIS should exist this may have consequences for research strategies. Where, on the one side, matter orientated biomedical research and treatments partially seems to stick in a cul-de-sac, on the other side alternatives with sometimes highly questionable methods, although not scientifically documented, report to achieve healing. An alternative entrance into medical research, implementing every kind of treatment, could be by questioning what the "informative content" of a treatment is and how this information interacts with the patients. In the next chapter it will be tried to formulate in more detail what implications an assumed existing BIS may have on medical thinking.

8.6 Literature

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9. Disease, medicine and the bio-informative state

9.1 The BIS and illness

Before discussing the connections between medical therapies and the BIS first a look has to be undertaken to determine the interrelations between illness and the BIS. In general illnesses are thought to be caused by external factors like viruses, bacteria, chemical substances etc., or internal factors leading to malfunctioning of body processes, for instance those caused by genetic code failures, auto-immune diseases etc. However a clear border between external and internal factors cannot always be drawn and sometimes no detectable factor at all can be made responsible for a disease. Another consideration is how to define the onset of a “disease”. As much as hot and cold both are a state of temperature without being able to draw a border between where hot starts and cold finishes, disease and health both are a state of “life”. Moreover, whereas hot and cold can be defined and quantified using a scale on a thermometer, there is no such a quantitative scale available for health and disease nor an instrument to measure it in one value. Even more, certain body conditions may not at all be perceived as ill until they are diagnosed as such, like for example cancer may grow over years without being detected and causing any symptoms. On the contrary diseases may be perceived without evidence for ill body conditions. Therefore the state of being ill also has something to do with consciously available information. As long as changes in the BIS caused by the interaction of pathogens with the body or malfunctioning own body processes, do not reach consciousness, no disease will be noticed, which does not mean these ill making processes are not happening. Influences on the BIS may be direct by biochemical reactions as well as indirect by the sense organs. At this point again the question must be asked what condition the BIS needs to be in to become conscious.

Another question which was asked in part one is why people sometimes get ill, while others under the same circumstances (like for example in contact with the same pathogens) don’t. Part of the answer was the physical condition these persons are in, but that this answer could not explain all. Assuming an existing BIS the other part of the answer might be formulated as follows.:

- external factors

The (biochemical) interactions taking place between a pathogen like a bacteria or virus, or chemicals etc. themselves introduce information in the body’s BIS whereby the strength of this informational input depends on the type of pathogen and the amount of information. The biochemical reactions themselves however are under influence of the existing BIS, which may be inhibiting as well as without influence or even stimulating.

- internal factors

Malfunctioning body processes are part of and happen within the body's own BIS environment. The balance between the strength of the informational input of the malfunctioning process and the (counteracting) strength of the BIS, may have an interfering influence in how far these malfunctioning processes can subsist.

Because the BIS is a construct of both physical and mental condition, a physical or mental condition alone never can be made solely responsible for a disease. Even the best physical or mental condition alone may not prevent the onset of a disease, even the worst may not lead to the onset of a disease.

What is also important in the assumption of the BIS as that information, although related to but not directly being a part of an ill-making factor, may interfere with the BIS thereby creating an informational state with protective or weakening properties. For example the news of a spreading flue epidemic might increase the susceptibility to become a flue, or the information of a new cure may induce healing.

9.2 The three basic therapies

In order to better understand the "informational content" of medical therapies, first basic similarities in the methods used all over the world should be determined. Secondary it then can be questioned how such therapies interfere with the BIS and visa versa.

The medical methods used can be summarised in three categories as listed below.

1. Mechanical manipulations

By mechanical manipulation one can understand any form of "touching" the body. This touching can be invasive with removing ill parts like by surgery, or less invasive like acupuncture, massage, douches etc.

2. Chemical manipulations

Chemical manipulations implement any form of adding substances to the body. These substances may be artificial chemical substances like drugs, natural substances in herbs, animal products or minerals or dietary. They may be swallowed, injected, inhaled or given in form of ointments.

3. Mental manipulations

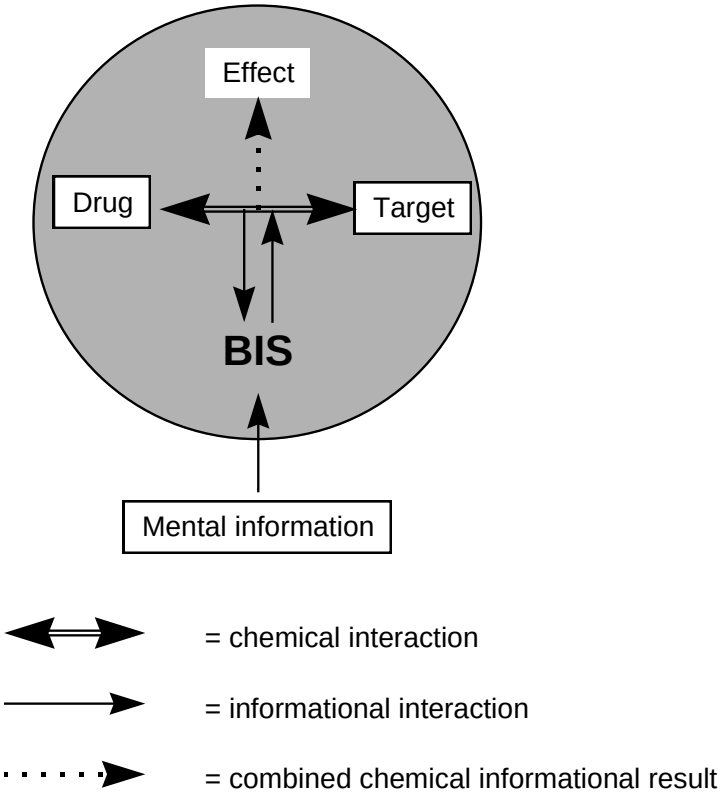
Whereas the above two manipulative therapeutic forms somehow directly change something within the body, mental manipulations only indirectly deal with the body. The therapeutic instruments comprise the stimulation of the visual and acoustic sense organs with sounds and images implementing words, conversations, rituals, spiritual healing etc.

What all three manipulative forms have in common is their interaction with the BIS, changing it, and being influenced by it. The first two forms by directly acting on matter-

matter interactions or fusions. The third, by indirectly presenting information which then is translated into the body on the level of matter-matter interactions. For instance consuming a drug will result in a biochemical reaction (fusion or interaction) thereby emerging information which becomes part of the BIS. How this biochemical reaction itself will succeed may be influenced by the existing BIS. The interactive strength of the BIS depends on other on-going processes, as well as on the strength of the added new emerging information from the introduced biochemical reaction. So it can be imagined that (see Figure 9–1):

- certain biochemical reactions are accompanied by such strong emerging “informational fields” that the influence of the BIS may be only weak and the chemical reaction will take place in favour of the expected result.
- the effect of biochemical reactions (with weak emerging “informational fields” ?) may be enhanced by the BIS.
- the momentary existing BIS is stronger than the informational input of the biochemical reaction and has a contra productive influence on the expected result.

Figure 9–1 **The influence of the BIS on drug-target interactions**



Because both mechanical and chemical manipulative therapeutic forms, alone or in combination, mostly take place in relationship with mental elements (an exception to this

may be when patients are in coma ?) the informative strength of the mental manipulative interactions may powerfully contribute to supply (and strengthen) the BIS with supportive or counteracting information.

9.3 What does medicine do?

Medical treatments consist of several elements as described above. The information which is applied from outside to a patient includes a “body” part and a “mental” part, both contributing to the BIS. On the other side an existing internal BIS is encountering these external informational fields. All the components as described in section one are part of the internal BIS: historical cultural influences with rituals, attitudes, religious beliefs etc., the biological interactive state of the nervous and immune system, the momentary conscious state with emotions, feelings, moods, stress, beliefs, expectations etc. Regarding an organism as a whole, one might wonder how, for example one more single biochemical interaction taking place in this huge complex soup of biochemical reactions, as can occur after taking a drug, is able to have such a powerful effect. Does not such a single reaction need the support of the whole system in order to be effective?

Many observations in medicine somehow seem to support the idea that medical treatment does not only rely on physical interactions:

- of drugs mostly information at the mental level is given: what the drugs are supposed to bring about in order to heal
- sometimes no effective substance is able to give the same effect, given the patient is given the information what the drug (=placebo) is supposed to do
- some therapeutic ideas rely on applying “purified information” like in homeopathy or solely acoustic and/or visual information (ritual or spiritual healing)

Administering whatever kind of therapy always results in the interaction of information from outside with that of inside. Which method fits the best for which person may well be determined by its existing BIS in combination with the method related added information, and not only by the method itself. Patients will put a given or chosen therapy in context to their individual beliefs and convictions (positively or negatively) thereby enhancing or inhibiting the effect of a certain therapy. A particular therapy not fitting into the individual BIS (including beliefs and convictions) may be less effective as the same therapy in an individual with a positive attitude.

➜ Medicine and informational surprise

One aspect of information related to medicine is the concept of information as described by Shannon and Weaver. According to them information is a quantity for surprise or the

amount of difference. This characteristic of information does seem to play an important role in medicine. First, in the case of habituation for instance, the constant intake of a drug may cause a decrease in effectiveness as no new “surprise” is added to the system. When informational content is defined by “difference”, the BIS can also be seen as a pool of differences which only is active and can take influence on on-going processes as long as these differences persist. Overriding the BIS with a big and constant amount of one sort of information can well lead to an overflow and lost of “surprise”, thereby decreasing the efficiency of the drug. Secondary the theory of surprise can be admitted to the finding that mostly patients seem to recover better at the start of a new therapy. The success of a therapy partially is given by the “new” of it. Patients for example who after using a given therapy do not completely recover and start utilising a new therapeutic method or medicine, in the beginning appear to benefit more.

➜ Medicine and excluded information

Another aspect of information is that mentioned by Nørretranders. His idea, that not the information itself is important but that what has been excluded to produce that information can well be translated into medicine. To illustrate this hypothesis consider all the available information not implemented in a drug or therapy but elicited by the receiver. First the form in which drugs are given, or the instruments used, may implement information which as such does not affect the physical effect: the colour, form and medium of a drug, the needle by which it is given etc. all induce information not directly relevant for the working mechanism of the drug or instrument (a big pill helps more, an injection even better, getting only a tee to drink means one is not as ill as if one needs an infusion etc.). Furthermore information is transmitted including for instance the knowledge that the drug/method healed others in the past or that the drug/method is safe with low risk of side effects (or the contrary). Even the production of drugs, instruments or the development of methods themselves are a process of excluding information, which in some form are included again when they start to “work”. A good example for this excluding information can be postulated for the theory of homeopathy. Diluting substances up to theoretically non detectable, non-present molecules purifies information by excluding (all non-relevant ?) information. It then can be supposed that the body reacts on this purified information by “recalling” the necessary excluded information inducing healing. The hypothesis that not the information which is given (in whatever form) but that what is transmitted in form of excluded information may help to understand why so many different therapies, trying to heal a single disease, have evolved so far. Could it be that not the therapy or drug itself but what is “meant” or “believed” it to do, which does not physically reside in the method or drug, that (at least partially) makes up its healing properties ?

9.4 Medical research and the BIS

9.4.1 Drugs

The momentary stand of modern biomedical research is to understand the physical properties of a substance and its reaction potential. The biggest problem this research is dealing with is that all biochemical processes they try to influence somehow are naturally, valuable and, for one or the other organism, essential processes. Biomedical drug research is mostly concerned with the biochemical reactions acting in diseases. The biomedical reactions in charge can be classified in such

1. not occurring thereby interrupting a certain step in a process, for instance when insulin is missing.
2. occuring but in the wrong way thereby producing false products, for instance when after a gene mutation a wrong protein is produced
3. naturally occurring at the wrong “time” and “place”, for instance the biochemical processes of viruses, bacteria or cancer cells
4. naturally occurring but in excess or in deficiency, for instance when too much or not enough of a neurotransmitter or hormone is produced

Aim of medical interventions is to add, substitute, inhibit, suppress or stimulate these biochemical processes. Whereas in the past these interventions were sought for by testing substances in trial and error experiments, lately drugs are designed on computers according to their structure and chemical properties. Furthermore the chemical structure of natural compounds, sometimes used over millennia with proven effect, is tried to be determined in order to chemically produce such substances. What is left out in all this research is information. Including information into medical research means to ask the following questions:

- What information will emerge when a substance starts to interact with body substances?
- How does this emerging information interact with the body’s BIS ?
- What effects can be expected from the BIS on the action of the substance ?
- How much “surprise” does the substance contain, and how long and how much will the effect of surprise persist?
- What excluded information does the substance contain which may be included when the substance gets in contact with the body?

Although some of these questions cannot be answered with today’s available methods, some can be. For example experiments can be designed investigating the effects of form,

medium, colour and application form of a drug thereby questioning the receiver what he/she thinks and beliefs this particular application form does. Other experiments might try to find out what added “mental” information[6] does effectuate on the drug and for how long a patient experiences a drug as “new” and effective. It can also be investigated because of what information patients choose for a certain drug or therapy when they have a free choice between different drugs or therapies for a certain disease, and what the effects of such a choice are on the efficacy of the drug or therapy.

9.4.2 Side effects

In modern clinical research it takes a long time before a drug is given to a patient. First the drug is designed or extracted from a natural medium, then it is tested for its chemical reaction patterns followed by tests on cell cultures, thereafter its effects and toxicity are tested on animals. Following clinical applications are designed in 3 phases. In phase 1 the toxicity of the drug is tested on mortally non treatable ill patients to establish an appropriate dosage, followed by phase 2 where a certain dosage then is tested for its effects on the disease it was designed for and the occurring side-effects. Phase 3 in the end is designed to test the drug against a test group of non-receivers (placebo) or those receiving a conventional drug to find out whether the new drug has any (better) result on the given disease. From the moment of introducing a drug into a cell culture the reacting drug interferes and adds information to an existing BIS. However, cell cultures and animals are not given additional mental information and therefore it is highly questionable whether the found results can be extrapolated to patients. What the BIS of a cell culture or an animal does to the biochemical reactions of a drug might be different from that of an informed ill patient. Even phase 1 and 2 clinical trials deal with different BIS situations as the real situation a drug is designed for. People without hope for improvement, mostly treated without success (phase 1 and 2) can be supposed to be in a total different BIS as a person first coming for treatment. Beside these people are informed with totally different mental information (you are part of an experiment, we can not heal you but you may help others to get better), then those in phase 3 (you are in an experiment and it is thought that the new drug may heal or will give better results then the conventional treatment). These different premises may count for the appearance of diverse side-effects. Side-effects not seen in animal experiments can appear differently at any phase of the clinical trial depending on the encountered BIS at that moment and also may be different from patient to patient.

[6] With mental information is meant all information which is given visually, linguistically and inter personally, by means of form, colour, ambience, atmosphere, conversation, media, inter personal connections, etc.

Another consideration concerning side-effects is that the information added to the BIS during a drug therapy and thereby changing it, may well influence non related biochemical processes. Furthermore the existing BIS of a person may stimulate or suppress chemical reactions a drug might initiate at unwanted locations, thereby influencing which side-effects will occur.

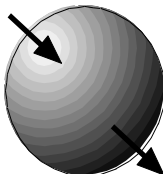
9.4.3 Non medicinal drug methods

The development of methods which do not use drugs is as old as the ones utilising drugs. Ancient methods such as acupuncture, massage or certain spiritual rituals also may have outlived after positive trial and error experiences. In the new ages methods were developed more based on advanced psychological and/or physiological knowledge, like hypnosis, relaxation, biofeedback or physiotherapy. Methods not implementing drugs somehow try to release internal information which may be blocked or hidden, or add external non “chemical” information missing in the body. Again none of these therapies is given without adding mental information, like explaining what is done and why, the ambience in which a therapy is given, the tools which are used etc. Whereas in certain situations it is tried to prevent a “clinical” atmosphere and add positive information, in others a missing “clinical” atmosphere may give inaccurate information, interfering negatively with a healing process.

9.5 Comment

Medicine is dealing more and more with two mutual forces. On the one side is the reduction of a disease to its biochemical components, thereby losing the view of a person as a whole. On the other side is the immense increase of information about a disease, which not only the physician is supposed to know, but the patient also gains knowledge of by means of the different media (newspaper, television, internet etc.). The reduction of a treatment to a biochemical or surgical intervention neglects the influence of information in the healing process. Whether a postulated BIS exists or not, it cannot be denied that somehow information plays a role in the healing process. Not only information given in forms of pills etc. but also the internal information in form of belief, confidence, trust, expectation and external information given by a doctor, enclosed drug information or even such given by the media, may affect the outcome of a therapy. Although the observation that mental states play an important role in a healing process, research so far has only considered the material component of these observations, trying to find material correlates for these mental states. That information and the informational content of mental states

might be one of many spectres of matter (according to physical pluralism) might offer a solution of how non material elements interfere and interact with material processes.
For medicine this hypothesis might initiate a search for what more information a treatment as a whole contains then only the treatment itself and what internal information is available in the patient which may interact with the given treatment. In the next chapter it will be described which information may be available and detectable with today's methods and if it is possible to incorporate the thought of information as an important component in healing in a more standardised way.



10. Can the theory be proven?

10.1 Theoretical science theories

The postulation of a hypothesis, mostly finds its beginning in personal subjective thinking. In order to become scientific this thinking needs at least to subdue the following rules:

1. The hypothesis must be testable in that perceivable, eventually measurable (quantified), predictions can be made.
2. The obtained knowledge must be explicitly described in natural language, mathematics, pictures etc. so that it becomes inter-subjectively available.
3. The hypothesis must be systematic so that it can be connected to existing scientific theories. The addition of new knowledge by the postulated hypothesis may not introduce knowledge conflicting with the existing knowledge.

Hypotheses and theories exist as long as they have not been falsified and replaced by new hypotheses. Strong hypotheses are those who seem implausible and yet appear to be true when falsification experiments fail to prove its incorrectness and procure evidence. A hypothesis or theory itself is not the truth but must be seen as a tool for thinking, it will be used as long as new tools become available. The aim of a hypothesis is to predict a certain phenomenon not predictable so far. In the following the above mentioned aspects of a hypothesis or theory, which must be fulfilled in order to become scientifically valuable, will be discussed for the postulated BIS.

10.1.1 Testability and predictable value of the BIS

➜ Testability

In chapter 8.2 the hypothesis was formulated that the bio-informative state (BIS) of an organism is the sum of all emerging information out of all on-going biochemical processes in an organism and has the characteristic and property of a force field, under the assumption that information is a elementary physical characteristic emerging from interactions, fusions and/or motions between/of elementary particles. The first element which has to be estimated is whether “information” is “something” physical or not. Up till now most of what is included and measured in physics somehow is made available for the human perceptive system. The existence of many supposed physical elementary particles for instance can only be proved indirectly by transforming their existence or the effects of their existence into a human perceivable form. The consequence out of this kind of proving is that instruments are made by humans to verify the existence of something humans belief to exist. For some postulated physical elements no such instrument could be designed yet, like for the postulated gravitons who convey gravitational force.

Information implies a controversy: on the one hand it is such a common thing everybody's brain, after perceiving it in many different forms, is daily dealing with, on the other side there is no way of directly measuring amount, strength or content of natural information. The notation "bit" as counter for amount of information is less suitable for natural biological information as only such information is processed physiologically which can be detected and handled by a system. Of an instrument designed to measure information must be expected that it makes information available for perception and that it tells something about the content of that information, starting from the smallest informational element up to the information of complex systems. In order to do so first an explicit definition of information must be found implementing content, meaning and form. By "creating" such a definition it may become possible to design an instrument measuring this definition. This may sound trivial as the human brain is an information processing and "measuring" instrument in the first place, however, humans only have knowledge of such information which becomes conscious and which can be perceived by the sense organs. The postulated BIS however is not primary available to consciousness although it is supposed to be in close contact with it. Maybe one day an instrument will be designed measuring emerging information in a biochemical process transforming it into a consciously available form ?

A hypothesis must not obligatory be testable by means of instruments producing values. Without using instruments the only (?) way to test for an existing BIS is by determining its conscious part. Detailed interviews and standardised questionnaires before, during and after a given medical therapy covering non-physiologically measurable 1) present information, 2) beliefs, 3) emotions, 4) confidence, 5) attitudes etc. in regard to the disease, the consulted physician, the given therapy and its outcome might reveal proof for the influence of these parts of the BIS. The only difficulty concerning consciously experienced and communicated information is not primarily its subjectivity but that it can never be known for sure that what is told is also what is thought and felt. Still to begin with, it would be highly interesting to make inventories of this available conscious information of the BIS and search for common reiterating elements as well as individual or ethical differences and associations with the given therapy.

➜ Predictable value

The next claim for a scientific hypothesis is that after testing it and becoming "values" , these values can predict a phenomenon or outcome. In case of the BIS this means that knowing the content of the BIS will predict for example the effect it has on newly introduced information whether in form of introducing chemical substances, by means of other kinds of manipulating the body or by pure mental information. As long as no

instruments are available to give a value to the BIS, this may be quite difficult to achieve. For the moment the only available instrument would be the inventory of consciously available information and compare it to medical records, therapy outcome etc. independent of which therapy is used.

10.1.2 Inter-subjective availability of the BIS

The request of inter-subjectivity for a postulated hypothesis or theory is of great importance to make the hypothesis universally accessible and testable. To overcome inter-linguistic variances and explanations the best way to describe a hypothesis is by means of mathematical, physical or chemical formulas. However, formulating theorems means excluding information: the simplest, shortest most universal and elegant formula or law itself does not contain much information but implies great amounts of excluded information. Information as an emerging as well as an influence taking factor never has been described in formulas so far and may become excluded information as soon as a theorem is formulated. To catch information in mathematical, physical or chemical formulas means to find a way of describing information without using information itself as the descriptor.

It may be hard to surpass this problem, even if physics would find a way to implement information as an elementary component of nature and describe its existence, a complex system as the BIS is far out of reach. Nevertheless, at least with using an objective language (as far as possible) and the awareness of the dilemma that information (must be) is used to describe information, it may be tried to find universal acceptance.

10.1.3 The connection of the BIS to existing scientific theories

The introduction of information as elementary part of our natural physical and biological world must not necessary be in conflict with existing physical laws. Instead capturing information into the existing theories might enrich these theories with answers about why things happen, compared to only describing how they happen. As already described in chapter 7.2, elementary particles are addressed to possess “knowledge” and “choice”, without this knowledge being formulated into a theorem. In biology, trying to understand processes by asking the question “why ?”, results in a long cascade of ever new questions of “why ?” only because it is unclear “where knowledge to do so resides” or in other words the element information is not been implemented. All physical and chemical theories presume information as given without questioning its existence.

The proposed characteristic of the BIS being a force field able to influence material interactions on first sight may be in conflict with the existing natural laws. First of all

because it is stated that “the mind”, a mental state or consciousness (or the proposed BIS) is “nothing” and nothing cannot do something (influence matter) because it lacks the energy to do so. However, physics so far has shown that “nothing” never is “nothing” and may as well be another state of “something” including its energy. When observed phenomena lead to assume that the existing theories only describe parts of them, the theories should be reviewed, renewed and completed with the missing components.

10.2 Research proposals

Even if it cannot be understood by today’s theories and laws how information is interacting with, produced by or resides within material interactions its existence and influence cannot be denied. In case of medicine understanding “information” may help to resolve what healing really is.

10.2.1 Different treatments, same information

One of the most interesting aspects of healing is that it can be achieved by so many different kinds of treatments. It would be interesting to find the commonness in these treatments and determine its importance in the healing process. Questions which could be investigated are:

- Internal available information
    - what does a patient know about a disease
    - what are his/her expectations when a physician is consulted
    - what is the connection between his/her beliefs and the treatment
- Non-physical (excluded) information of the treatment
    - what information does a patient “include” in a given therapy
    - what influence has the ambience of the clinical setting
    - what influence have previous clinical experiences
- Informational interaction between physician and patient
    - what does the patient tell the physician
    - what information does the physician give
    - what is the hierarchy between patient and physician

Independent of the given treatment the answers to these question can be compared with therapy outcome and maybe correlations can be found.

10.2.2 Same treatment, different information

Today modern western medicine is practised almost all over the world as much as ancient Asian or other non-western medical practises become available in Western countries. It may be questioned in how far a certain therapy has the same informational content for the patients it was originally developed for and those using such a therapy as “alternative”. Whereas “alternative” therapies in western countries become more and more popular, some of them are not at all “alternative” in the country of origin. It would be fascinating to investigate the informational content of a given therapy for different users and compare these findings with therapy results. Principally the same questions as mentioned in chapter 10.2.1 can be asked to reveal insight.

A second issue concerning a same treatment with different information is the fact that information availability concerning diseases and treatments is extremely divergent for different layers of the population as well as between different countries. Texts, from specific patients information bulletins to those in women’s magazines, may inform about a disease extremely differently and with fast changing opinions. Media like television, newspapers, popular scientific magazines etc. available for some but not all people may scatter the most contradictory information about health and disease upon the population, whereas others never come to this kind of information at all. Should not these informational influences be investigated? What the effects of such information are on the individual inner beliefs and trusts are unknown so far. In addition, with the increasing informational (over)flow it seems time to investigate what and how much a patient knows as well as he/she should know and what the effect of this knowledge is on the healing process. Furthermore these investigations should not be restricted to the side of the patient but also be investigated for physicians themselves, as they can hardly follow the increasing amount of information.

10.3 Comment

During the course of evolution consciousness is one of the characteristics humans have developed which allows the active search for understanding life and nature. The emerging understanding can be seen as a product of its own being: the way life and nature is understood is dependent on the thoughts produced by this life and nature. From the moment on these thoughts have been documented it has become possible to follow the shifts in thinking and understanding in relation to dominating religious, political, economical and natural environment. The above formulated thoughts on information, the BIS and its influences on material processes therefore are no more than one out of many

emerged ideas which has to be placed in the momentary context of the existing “world” view. Information is a rather new component of the modern world, it is a “concept” without a clear definition but with (for many) an enormous importance. Information is taken for granted in many physical and chemical concepts without questioning its being as such. Still it is undeniable that information has influence on living organisms and is part of the unconscious as well as the conscious body. The proof of the existence of a hypothesised BIS may be difficult to achieve. To start with, “information” must be defined in a form not using “information” itself for the definition. The controversy “information” includes is hard to overcome. So far, as a physical property information is “nothing”, it does not exist in a “detectable” manner. The only detectable part of information is its carrier, whether a wave, electric impulse, molecule, letter etc., which can be perceived in one way or the other by sense organs. The perceiving process then changes something in the organism, however, how and which changes take place is not only determined by the physical and biochemical properties of the interacting matter but also by the information which is transmitted (or emerges). At this point information becomes “something”. If ever a way should be found to determine information into a reproducible value, one might ask what this value can tell more. In case of the BIS it is even highly questionable if this "subjective inner knowledge" should become available in order to fit into experiments which in the end are designed to “manipulate”, without anybody being able to determine which “manipulation” is advantageous and which isn’t.

Whereas the BIS might remain a pure speculation, information in medicine should be considered as an important ingredient of the healing (and ill making) process and be taken as a subject of investigation. Information not only can turn out to be the mutual factor shared by all medical methods in the world, but also a powerful component influencing a therapy’s outcome.

10.4 Literature

. 129 Grind v.d.W. “Natuurlijke intelligentie”, first edition, Uitgeverij Nieuwezijds, Amstersdam 1997

Personal comments

During my training as a biologist I have always been interested in complex systems and searched for connections and relations between seemingly isolated phenomena. My personal interests brought me into an at that time aberrant and non practised direction of biology which later was called “human biology”. Biologists didn’t like “humans” as the subject for their studies because they were unpredictable and didn’t fit in what they thought were controlled experiments. My first project working with human material was on patients undergoing open heart surgery for coronary bypasses, investigating their immune status. It was this project which showed me that what we were measuring couldn’t only be due to the surgery itself (as we tried to proof) but must have been the result of the whole complex leading to the necessary for a coronary bypass in the first place. No patient started with similar values, no patient showed similar effects on his/her immune status during and after the operation. At this point I started wondering if we were asking the right questions and became quit critical towards my own and others work.

In the following years I became familiar with cancer research and diagnosis. One of the most emphasised subjects I was involved in were prognostic parameters. For most cancer types it has been tried to determine “the” prognostic factor, in the end resulting into many prognostic factors for one cancer type and a different prognostic factor map for every patients or even different tumour cells within one patient. None of the prognostic factors has ever been found to have a 100% certainty score and with new factors being implemented in the prognostic factor map no black or white answer ever seems possible. People only partially seem to behave according to their prognostic values when it comes to cure or death. Reading more about treatments for cancer yielded in a same kind of view: no treatment seems to result in a 100% certainty for cure.

During the time of my study and thereafter I tried to incorporate new points of view into this “scientific” reductionistic way of thinking. One of my fields of interest became psychoneuroimmunology as this seemed the first scientifically based research area integrating “mind” into body processes and connecting body systems thought to be separately functioning so far. Over the years however even PNI research has remained

basically materialistic and not able to solve the problem of the influencing “non-materialistic mind”. The on-going decade has become the decade of the brain and consciousness in the hope to finally understand consciousness and solve the problem whether mind can influence the body or is only a product of the body without influence. Although it is clear that only isolated subjects can be the topic of investigation and step by step may fill in the whole, I keep on wondering if our way of thinking is altogether correct . As I see it now the crucial element which has not been incorporated into all scientific thinking is the element “information”, what it is, what it does and what it means.

As I pointed out in the first part of the manuscript, illness and healing are under influence of external elements like historical, cultural and religious predestinations which have lead to the world wide most diverse healing methods, as well as under physiological and mental internal elements. Only a minor part of all these elements directly embody material processes. The majority are “mental” or “informative” which have to be translated into material processes in order to be affective (?). Whereas some ancient and/or so called alternative medical practises rely partially or even totally on the transmission of information in order to heal, biomedicine does not consider information as an important element in research or treatment. It is my conviction that information might be one of the key elements in understanding healing and that material and mental processes are connected by this information. With today’s available “technical” methods it still may be hard to investigate my ideas. Nevertheless a start can be tried when modern science accepts that a crucial component is missing in their material based experiments, a component which is so obviously available.