Mind over Matter in Modern Medicine

PART 1: Placebo

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Intro | Evolution | APR | Psyche | Conclusion

Trigger (1/2)

Beecher 1955 …. The Powerful Placebo

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PLACEBOS BECOME RESPECTABLE

p.4: In 1955, Beecher summed up the new view of placebos in an influential article published in the *Journal of the American Medical Association*[5] Entitled '**The Powerful Placebo**', the article claimed that placebos could 'produce gross physical change', including 'objective changes at the end organ which may exceed those attributable to potent pharmacological action' …. The placebo effect was born ….

p.10: Beecher argued that all kinds of treatment, even active drugs and invasive surgery, produced powerful placebo effects in addition to their specific effects ….

p.12: …. placebos are extraordinary drugs. They seem to …. work in at least a third of patients (usually) and sometimes in up to 60 per cent [13] …. A respected biologist states that 'placebo medical procedures have proved to be effective against …. chronic pain, high blood pressure, angina, depression, schizophrenia and even cancer'." A leading authority on alternative medicine goes even further, claiming that 'the range of susceptible conditions appears to be limitless'.[15]

p.13: to calculate the true placebo effect, the rate of spontaneous remission shown by those receiving no treatment at all must be subtracted from the observed placebo effect (i.e. requires a reference group in which nothing is done!) ….

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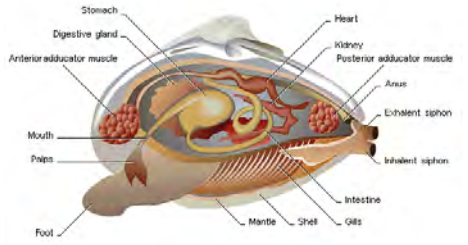
Early Organisms (1/7)

Origin of Immunity

- Porifera possess phagocytes;
- Early mollusc did not form a discrete brain; neurons aggregate freely throughout body;
- Mechanical stimulation causes molluscan body to contract …. No entity present that limits communication b/w neurons;
- Predation of a molluscs triggers the same neurons (release of IL-1 binds to motor neuron);
- Molluscan neuronal network acts as a SENSORY ORGAN;

Evans, 2003



- BB-barrier in higher organisms prevents infiltration of pathogens / toxins;
- Evolution of complex ways to bypass BB-barrier;
- immune conditioning: a by-product of the immune-brain interaction?

Immune conditioning relies on a very complex set of mechanisms that allow communication between the immune system and the brain, and it is highly improbable that such complex mechanisms would ever evolve simply by random changes in gene frequency …. Immune conditioning might be a mere side-effect of the fact that the very first brains evolved in close contact with the immune system ….

p.106: Immune systems are found in the most primitive of multicellular creatures. Sponges, for example, have phagocytes …. which recognise bacteria and participate in wound healing. These primitive immune cells defend sponges against infection and tissue injury without any help or interference from neurons, which sponges do not possess. By the time neurons began to evolve, therefore, an immune system of sorts was already well established …. In the first molluscs …. which appeared around 550 million years ago, the neurons did not form a discrete brain, but were rather clumped in a number of clusters throughout the mollusc's sinewy body.

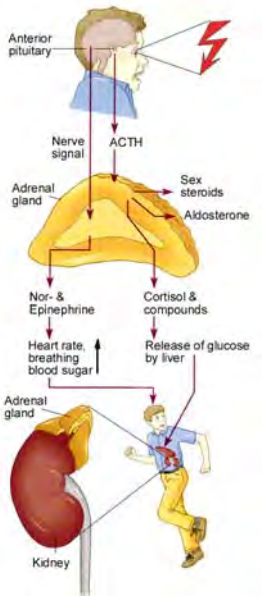
p.107: There was therefore nothing to stop these neurons communicating freely with the immune cells …. When a mollusc comes into contact with a predator, the withdrawal reflex is triggered by the same signalling molecules that cause inflammation in mammals. First, the predator is detected by immune cells on the surface of the mollusc, which release IL-1. The IL-1 then binds to receptors on the mollusc's motor neurons, which initiate movement away from the threat. The immune system in molluscs thus functions as a kind of sensory organ. **Some biologists have suggested that the immune system also functions as a sensory organ in higher animals, including humans**.[10] …. The neurons continue to speak in the same language, passing the same ancient signalling molecules back and forth. The fact that these molecules are classified by humans into neurotransmitters and immuno-transmitters is largely a historical accident …. The same molecules that allow neurons to talk to each other also facilitate talk between neurons and immune cells. The same goes for the molecules that allow immune cells to communicate with each other.

p.108: The walls of blood vessels supplying the brain evolved special mechanisms to prevent the flow of all except the very smallest molecules from the blood to the brain. The blood-brain barrier, as it is called, protected the increasingly complex and vulnerable brain from all sorts of toxins and pathogens …. That complex ways of bypassing this barrier then evolved — such as the chemical cascade described in Chapter Three, which allows a build up of IL-1 in the bloodstream to trigger an increase of IL-1 in the brain indirectly …. By this stage, a stunning variety of immune responses had evolved that could not function harmoniously without cerebral supervision .... It is, therefore, perfectly possible that immune conditioning is simply a by-product of the immune-brain connections etched so deeply into the fundamental vertebrate body plan ….

Source: http://www.earlham.edu/~burksje/bananaslug.htm

Evans D. (2004): PLACEBO - Mind Over Matter in Modern Medicine; Harper Collins Publ.; London - UK

HPA (2/7)



Function or By-product

- i) adaptation designed by natural selection or i) not a true function of the mechanisms that produce it - a byproduct?

- fight-flight response evolved by co-opting the biological systems underlying the acute phase response;
- innate immune response to infection and the fight-flight response to large predators activate the same immune-brain circuits
- fever is also triggered by the sight of a dangerous animal;
- increased risk of infection in combat w/ other animals. Legs get scratched while running; skin gets ripped when fighting;

Maier & Watkins, 1998

Postlethwait & Hopson, 1995

FUNCTION OR BYPRODUCT?

p.98: The first possibility is that the placebo response is an adaptation designed by natural selection. In other words, the mechanisms that produce the placebo response allowed those of our ancestors who possessed such mechanisms to survive and reproduce more successfully than those who lacked them (is it really a question of evolution?) …. What particular advantages did the capacity to respond to placebos confer on those who possessed it? The other possibility is that the placebo response is not a true function of the mechanisms that produce it, but a mere by-product, like the soft sounds made by the beating heart …. The human body is riddled with design faults which natural selection has not yet been able to eliminate.

p.99: The fact that the windpipe leading from our noses to our lungs, for example, intersects with the digestive tract leading from our mouths to our stomachs, means that we are at risk of choking to death ….

THE ORIGINS OF STRESS

p.138: *Steve Maier* and *Linda Watkins* claim that the fight-flight response, which enables vertebrates to respond to large predators, evolved by co-opting the biological systems underlying the acute phase response that had already evolved, millions of years before[19] …. Both the innate immune response to infection and the fight-flight response to large predators activate the same immune-brain circuits …. The risk of infection is increased …. in combat with, another animal. Legs get scratched while running, and skin gets ripped when fighting

p.139: This makes good sense, since cortisol breaks down the body's fat reserves into glucose that provides vital energy …. Many apparently arbitrary features and design faults are only explicable in the light of this makeshift history. For example, it might seem odd that people get hot and sweaty when faced with a dangerous animal. Yet this psychological response is understandable in the light of the evolutionary history of the HPA axis …. The fact that fever is now also triggered by the sight of a dangerous animal is a by-product of this evolutionary legacy ….The risk of infection is increased …. in combat with, another animal. Legs get scratched while running, and skin gets ripped when fighting ….

Source: Maier SF, Watkins LR. (1998): Cytokines for psychologists: implications of bidirectional immune-to-brain communication for understanding behavior, mood, and cognition. Psychol Rev. 105(1):83-107.

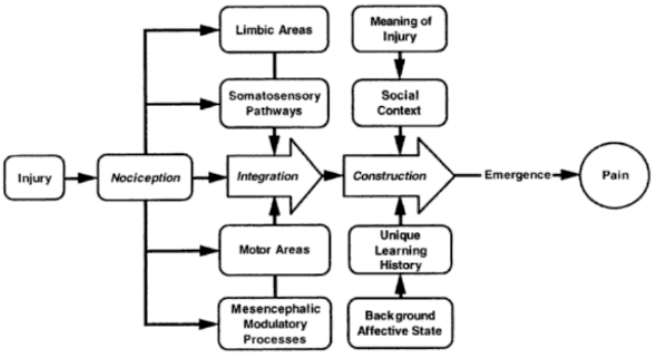
http://psycnet.apa.org/index.cfm?fa=search.displayRecord&uid=1997-42747-004

Pain (3/7)

Pain as a Need State

- relevance of social support to pain relief;
- Pain is a vital protective mechanism - those who lack it do not survive very long;
- Alone, and the protective value of pain outweighs the disadvantage of slowing down the healing process;

Wall 1999



Papagallo, 2004

PAIN AS A NEED STATE

p.111: Patrick Wall …. argued that the mechanisms underlying pain …. in humans is also influenced by a whole range of factors in the social environment. Among these factors, Wall claimed, is the availability of medical help. This, at least, seems to be what Wall meant when he claimed that pain is a 'need state', like hunger and thirst.[13] Need states are terminated by a specific consummatory act: hunger by eating, thirst by drinking. Pain, too, can be terminated by various 'consummatory acts'…. Crucial to Wall's argument, however, is that pain can sometimes be terminated simply by care and attention from others ….

p.112: Wall's claim about the relevance of social support to pain relief is supported by the studies …. that investigated the anti-inflammatory effects of fake ultrasound. One of these studies found that the placebo response was only triggered when the fake ultrasound was applied by *someone else.* When exactly the same physical stimulus was applied by the patients to their own faces, the swelling was not reduced. This suggests that the mere provision of social support can be sufficient to trigger the placebo response …. Pain is a vital protective mechanism, and those who lack the capacity to feel pain do not survive very long …. High levels of pain can actually slow down the healing process. When one is alone, the protective value of pain might outweigh the disadvantage of slowing down the healing process, but when others are taking care of you, the cost-benefit ratio may change. In particular, when others can protect you, pain might not be so vital …. Self-defence is unnecessary when other people are around to do the defending for you ….

Source: Pappagallo M. (2004) The neurological basis of pain. McGraw-Hill, p.163

Prehistory (4/7)

Primates & Medicine

- A chimpanzee takes care of *himself* when ill or injured ….
- by consuming plants with medicinal properties;
- by dabbing leaves on bloody wounds;
- Chimpanzees spend long hours picking the ticks off each other's backs ….

…. socially applied preventative medicine?

Evans, 2002

THE PREHISTORY OF MEDICINE

p.109: By the time the human lineage began to diverge from that of the chimpanzees, some five million years ago, the capacity for immune conditioning was well established …. They found, quite by chance, that they could train their immune systems to respond to certain stimuli in ways that felt quite beneficial. These stimuli dabbing leaves on each other's wounds, perhaps, or giving each other special herbs when sick — were the origins of medicine ….

p.110: Primatologists have observed many cases in which a chimpanzee takes care of *himself* when ill or injured …. such as consuming plants with medicinal properties or dabbing leaves on bloody wounds, but they have never seen one chimp providing this sort of medical assistance to another. Chimpanzees do spend long hours picking the ticks off each other's backs, which could, perhaps, be regarded as a kind of preventative medicine, but *therapeutic* medicine seems to lie outside their behavioural repertoire …. We know, then, that medicine - the provision of special care to the sick by others - must have originated some time between five million and ten thousand years ago ….

Source: Evans D. (2002) Pain, Evolution and the Placebo Response. Behavioral and Brain Sciences 25 (4); 459-460.

Immune Conditioning (5/7)

Humans & Medicine

- Group A: γ-interferon injection paired with oral administration of PG* (gradually fewer injection; i.e. no injections at end of study);
- Group B: saline-injection paired with oral administration of PG*;
- Group C: γ-interferon injection alone;

(*) Conditioning stimulus: propylene glycol (PG)

Blood-serum concentrations of:
quinolinic acid & neopterin
(markers of immune-activation):

Results:

Group A: mean serum conc. signif > Grp.C;
Group B: no immune response;
Group C: gradual decrease of mean serum concentration;

Longo et al., 1999

p.104: Conditioned enhancement of the immune system has also been demonstrated in humans …. Over four weeks, the first group was given a course of oral placebos, each of which was accompanied by an injection of gamma interferon, which stimulates macrophage activity. The second group was also given the course of oral placebos, which were also paired with injections of gamma interferon to start with, but were progressively weaned off the injections so that by the last week they received only the placebo. At the end of the study, the second group had higher levels of macrophage activity than those who had received the gamma interferon all along[8] ….

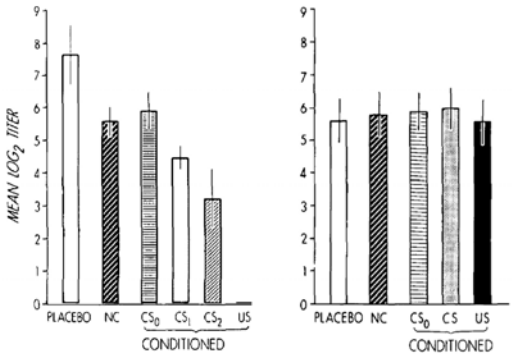
p.105: Volunteers were conditioned to associate substances from different-coloured vials with different immune responses.[9] At monthly intervals, material from a green vial was applied to one arm while another substance from a red vial was applied to the other arm. Unknown to the subjects, the green vial contained tuberculin, which is a harmless protein derived from the bacillus that causes tuberculosis, while the red vial contained saline. Tuberculin does not itself cause the disease, but in those who have been exposed to the bacillus beforehand, it triggers an inflammatory reaction. After six months, the contents of the vials were secretly reversed. This time, the arm to which the tuberculin was applied did not produce nearly such a vigorous inflammatory response. The volunteers had been conditioned to expect no inflammation to result from the material in the red vial …. the arm painted with the saline did not generate an inflammatory response, even when it came from the green vial.

Source: Longo D L; Duffey P L; Kopp W C; Heyes M P; Alvord W G; Sharfman W H; Schmidt P J; Rubinow D R; Rosenstein D L (1999). Conditioned immune response to interferon-gamma in humans.Clinical immunology; 90(2):173-81 …. We determined whether a classical conditioning paradigm may be used to condition immunologic responses in normal human subjects receiving an optimal immunostimulating dose of recombinant human interferon-gamma (rhIFN-gamma). We conducted a placebo-controlled, double-blind study of 31 normal volunteers in order to determine whether an initially immune-neutral stimulus, oral propylene glycol (PG), could eventually elicit an immune response as a consequence of its being paired with a known immunostimulatory dose and schedule of rhIFN-gamma. Subjects were randomly assigned to one of three groups: (A) rhIFN-gamma injections paired with PG; (B) normal saline injections paired with PG; (C) rhIFN-gamma injections alone. During the 4-week study, subjects received progressively fewer injections so that, by the final week of the study, no injections were given and groups A and B received only PG. The principal outcome measures were serum concentrations of quinolinic acid (QUIN) and neopterin, two nonspecific but sensitive markers of immune activation, and expression of Fc receptors (CD64) on peripheral blood mononuclear cells. RhIFN-gamma injections produced significant and predictable alterations in each of the measured immune parameters. No group B subject made an immune response. Mean serum QUIN levels were significantly higher at the end of week three for subjects in the experimental condition (group A) than for subjects receiving rhIFN-gamma alone (group C) despite receiving identical doses of rhIFN-gamma. Similarly, the predicted decay in mean serum neopterin levels from the end of week 1 to the end of week 2 was seen in group C but not in group A. The exposure of group A to PG blunted the decline of CD64 expression in week four. The data suggest that the pairing of an unconditioned stimulus (rhIFN-gamma) and a conditioned stimulus (PG) permits the conditioned stimulus alone to prolong a cytokine-induced response in normal humans.

Immune Conditioning (6/7)

Humans & Medicine

- Cyclo-phosphamide (CPA) injection paired with consumption of sweetened water;
- suppression of immune system (nausea, vomiting)
- Injection of SheepRBC induced high death rate of rats;
- substitution of CPA with saline solution paire with consumption of sweetened water;
- Conditioned rats auato-suppressed their immune-system - increased death rates!



treated with CPA — treated with LiCl

Hemagglutination titers 6 days after SRBC injection

Aden & Cohen, 1975

IMMUNE CONDITIONING: If we found that the placebo response was widespread among mammals, this would be good evidence that it evolved much earlier, no later than the time when the last common ancestor of all mammals walked the earth …. To be specific, rats, mice, guinea pigs and dogs have all been shown to be susceptible to a phenomenon known as *immune conditioning* ….

p.100: By repeatedly injecting rats with cyclo-phosphamide (a drug that induces nausea) whenever they drank sweetened water, Ader and Cohen succeeded in training the rats to avoid sweet water. Unfortunately for the poor rats, however, it seemed that their immune systems had been affected too, and they began to die in unexpectedly large numbers. Besides inducing nausea, cyclophosphamide also suppresses the immune system, so Ader and Cohen had inadvertently conditioned the rats to suppress their own immune responses whenever they drank the sweet water .... After conditioning the rats by pairing sweet water with injections of cyclophosphamide, they injected them with sheep red blood cells, which, although harmless, provoke an antibody response …. The rats had learned that injections after sweet water suppressed their immune systems, and so they responded by suppressing their immune systems themselves when faced with what they thought was the same situation again — even though it was not, in fact, exactly the same situation, since the cyclophosphamide had been replaced by saline. The rats had, so to speak, been tricked into suppressing their own immune systems ….

p.101: Besides destroying cancer cells, chemotherapy has the unfortunate side-effect of destroying the body's own immune cells too, and so is not unlike cyclophosphamide in suppressing immune activity. Not surprisingly, the body resists chemotherapy, and reacts to it with feelings of nausea and consequent vomiting. In the 1980s, doctors noticed that cancer patients who had been receiving chemotherapy would start to feel nauseous and even vomit on arrival at the hospital, before they had been given that day's dose. The doctors guessed that the conditioned vomiting might also be a symptom of conditioned immunosuppression …. One group of researchers measured various indices of immune activity in a group of women cancer patients several days before their scheduled chemotherapy session, and again in the hospital just before treatment.[6] While there was no change in some of these measures, there were significant reductions in others. The association of the hospital environment and the chemotherapy had become so ingrained that the mere sight of the place (or perhaps its smell) was enough to trigger a decrease in immune activity ….

Left image: Hemagglutination titers (means +/- SE) obtained 6 days after ip injection of antigen (SRBC). NC = nonconditioned animals pro- vided with saccharin on Day 3 or Day 6; CSo = conditioned animals that did not receive saccharin following antigen treatment; CS1 = conditioned animals given one exposure to saccharin on Day 3 or Day 6; CS2 = conditioned animals exposed to saccharin on Days 3 and 6; US = conditioned animals in- jected with cyclophosphamide following treatment with antigen.

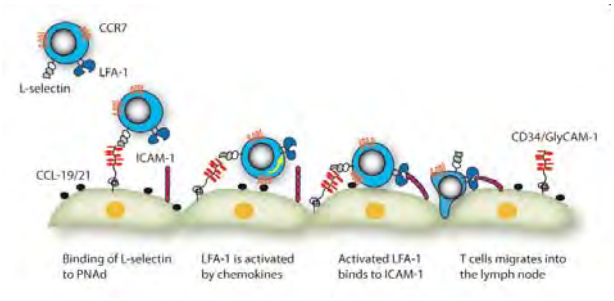
Right image: Hemagglutination titers (means +/- SE) obtained 6 days after ip injection of SRBC in animals conditioned with LiCl as the US. NC = nonconditioned animals; CSo = conditioned animals that did not receive sac- charin following antigen treatment; CS = conditioned animals given three exposures to saccharin; US = conditioned animals in- jected with LiCl following treatment with antigen.

Source: Ader R. & Cohen N. (1975). Behaviorally conditioned immunosuppression. Psychomatic Medicine 37: 333 - 340;

Immune Trafficking (7/7)

Humans & Medicine

- Immune conditioning is much broader than placebo response;
- toxins in the bloodstream: immune resources are withdrawn from peripheral circulation and locked them away e.g. in thymus, lymph nodes;



- certain circumstances favor diseased state rather than recovery; e.g. shock, danger, imuno-suppression (production of antibodies is energy-intensive);

Humphrey, 2000

IMMUNE TRAFFICKING

p.115: If the placebo response is simply a by-product, then it is probably a by-product of immune conditioning. …. That immune conditioning is a much broader category than the placebo response. All sorts of immune activity can be conditioned, including activation of the inflammatory response (s.p.82-87) ....

Any animal, then, that could respond to the presence of toxins in the bloodstream by withdrawing its immune resources from peripheral circulation and locking them away safely in organs such as the thymus, would have an advantage over animals that could not. There is, in fact, growing evidence that such 'trafficking' of white blood cells between the peripheral circulation and the central organs of the immune system, does occur. The immune system …. can regulate the proportion of various kinds of white blood cells that circulate freely around the body and the proportion of those that are locked up in the thymus and the lymph nodes ….

p.116: We can measure the number of various kinds of white cells in the bloodstream, and this number drops sharply in response to various conditioned stimuli …. Conditioned immuno-suppression simply involves moving certain immune agents out of the bloodstream and into the safety of various organs ....

Thus, it seems that suppression of certain immune agents is a controlled process underlying the subconscious regime of our mind;

Source: Humphrey N. (2000) Great expectations: the evolutionary psychology of faith-healing and the placebo effect. The Mind Made Flesh: Essays from the Frontier of Evolution and Psychology; Oxford University Press: 255-285;

http://www.landesbioscience.com/curie/images/chapters/01Maiese1color.gif

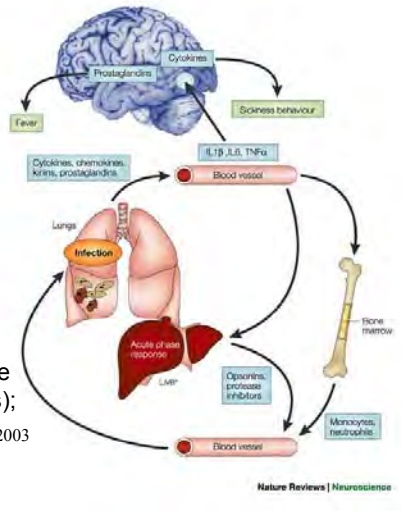
APR (1/4)

Acute Phase Response (APR) & the role of cytokines in infection / injury e.g.:

- Interleukin (IL-1β) diffuses i/o surrounding tissue;
- production of prostaglandins;
- BB-barrier - activation of neurons & microglia;
- fever, lethargy, apathy, anxiety, loss of apatite etc.;

Similarly, anxiety disorders are bound up with the immune system too (phobias, panic attacks, all stress symptoms);

Perry et al., 2003



THE ACUTE PHASE RESPONSE

p.45: Western medicine recognised the four signs of inflammation as swelling, redness, heat and pain … Besides these physical changes, there are also important psychological ones, including lethargy, apathy, loss of appetite and increased sensitivity to pain — a suite of symptoms that are collectively known as 'sickness behaviour'[1] …. The lethargy that commonly ensues after infection, for example, was thought to result from debilitation, as if the body had simply run out of energy …. They are actively produced by the body itself as part of the healing process. They may feel unpleasant, but they are actually good for you. In fact, feeling unpleasant is a vital part of their function ….

p.48: Many different cytokines are involved in the acute phase response …. Known as inter-leukin-lβ (IL-1β) …. The IL-1β diffuses into the tissue surrounding the damaged cells, where it triggers a second wave of cytokines which cause other types of immune cell such as neutrophils and monocytes to migrate to the injured site.[4] The IL-lβ released by the macrophages also enters the bloodstream, where it is carried to the brain.[5] …. First, the IL-lβ molecules attach themselves to …. surface of the cells in the blood-brain barrier …. that eventually leads to the manufacture of a molecule known as prostaglandin E2, which — unlike IL-lβ — is capable of passing through the blood-brain barrier. When it enters the brain, prostaglandin E2 activates receptors on both neurons and microglia (immune cells in the brain), which can then initiate the other components of the acute phase response: fever, lethargy, apathy, loss of appetite, anxiety, and increased sensitivity to pain in other areas of the body ….

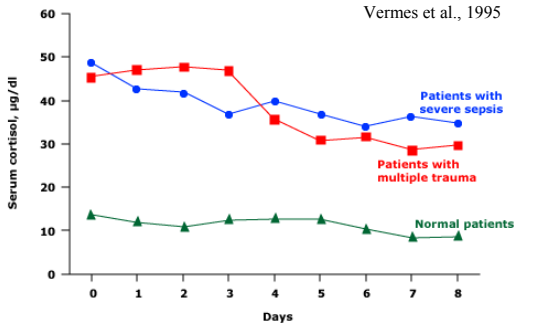
p.54: Anxiety disorders, too, are bound up with the immune system in similar ways. In phobias and panic attacks the body's natural stress response is pushed into overdrive, and elevated levels of the stress hormone, cortisol, are found in people with these disorders. Increased levels of cortisol are also found in people with depression …. Many people with depression experience intermittent bouts of anxiety, and many people with anxiety disorders report long episodes of low mood. In technical terms, there is a high degree of co-morbidity between depression and anxiety ….

Source: http://www.nature.com/nrn/journal/v4/n2/fig_tab/nrn1032_F2.html

Cortisol (2/4)

Cortisol - a stress-related hormone …. e.g. Hypothalamus-Pituitary-Adrenal (HPA) axis

- keeps levels of IL-1β under control (neg. feedback loop);
- HPA-released amounts of cortisol in response to stimulation by IL-1β are much smaller than those used in anti-inflammatory drugs, (here cortisol may actually enhance inflammation);
- inhibition of neuronal growth;
- administered in organ transplantation;
- Emotion – the language of cells;



THE PARADOXES OF CORTISOL

p.55: Some immunologists claim that, in the normal person, cortisol acts as a negative feedback mechanism, regulating the inflammatory response by keeping levels of IL-1β under control[11] …. The inflammatory effects of IL-1β are apparent within minutes, allowing the body to respond very quickly to injury and infection ….

p.56: The cortisol arrives just in time, it has been suggested, to prevent the inflammatory response from reaching extreme levels. The circuit therefore functions as a negative-feedback loop. This theory is certainly plausible, but there are also problems with it. Specifically, the amounts of cortisol released by the HPA axis in response to stimulation by IL-1β are much smaller than those used in anti-inflammatory drugs, and at these levels cortisol may actually enhance inflammation[12] The evidence is mounting that the same family of closely related mechanisms underlie pain, swelling, ulcers, depression and anxiety. These mechanisms are the very same as those involved in the acute phase response. This suggests that the reason placebos can alleviate some conditions but not others is to be found in the workings of the immune system. The Hypothalamus-Pituitary-Adrenal-Axis (HPA) …. When there are no threats, the HPA axis is inactive and growth flourishes …. The stress hormones released into the blood constrict the blood vessels of the digestive tract, forcing the energy-providing blood to preferentially nourish the tissues of the arms and legs that enable us to get out of harm's way …. The visceral organs stop doing their life-sustaining work of digestion, absorption, excretion and other functions that provide for the growth of the cells and the production of the body's energy reserves …. Activating the HPA axis also interferes with our ability to think clearly …. when you're frightened you're dumber …. Exam stress paralyzes these students …. We live in a "Get set" world …. Our daily stressors are constantly activating the HPA axis, priming our bodies for action …. Almost every major illness that people acquire has been linked to chronic stress [Segerstrom and Miller 2004; Kopp and R6thelyi 2004; McEwen and Lasky 2002; McEwen and Seeman 1999] …. More researchers are pointing to the inhibition of neuronal growth by stress hormones as the source of depression …. Depression is caused when the brain's stress machinery goes into overdrive. The most prominent player in this theory is the hypothala-mic-pituitary-adrenal (HPA) axis" [Holden 2003] …. Stress hormones are so effective at curtailing immune system function that doctors provided them to recipients of transplants so that their immune systems wouldn't reject the foreign tissues ….

Image: Vermes, I, Beishuizen, A, Hampsink, RM, Haanen, C.(1995) Dissociation of plasma adrenocorticotropin and cortisol levels in critically ill patients: possible role of endothelin and atrial natriuretic hormone. J Clin Endocrinol Metab; 80:1238.

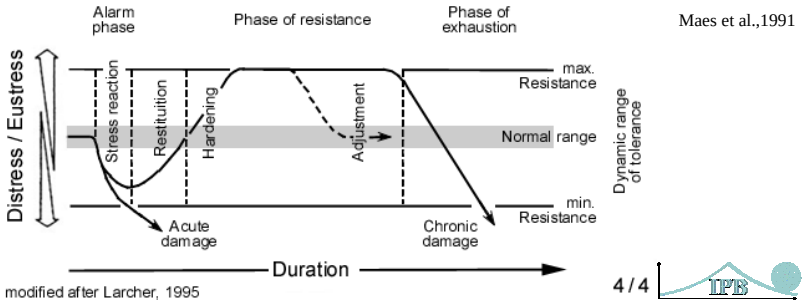
Source: Postlethwait J.H. & Hopspn J.L. 1995. The Nature of Life, 3rd ed. MacGraw-Hill.

Lipton B. (2005) Biology of Belief. Elite Books p.148-152

Stress (3/4)

Chronic activation of the APR

- baboons: threat from dominant alpha males - immune system continually primed by bursts of cortisol - quick response to scratches - **sickness behaviour becomes a way of life**;
- humans: backbiting is metaphorical - biological effects very similar, leading to the same state of chronic activation of the APR;
- IL-1β-production by macrophages in severely depressed people;
- Overdriven stress-response in patients with phobias & panic attacks;



p.140: So it may well be adaptive to prime the innate immune system for instant response on those occasions when wounds are more likely …. For baboons at the bottom of the social hierarchy, the most immediate threat of injury may not be from a predator, but from the dominant baboons in the same troop …. The immune system continually primed by bursts of cortisol so that it can respond quickly to potential infections in the scratches caused by the surly alpha males …. The continual activation of the acute phase response can lead eventually to a state of chronic inflammation, in which **sickness behaviour becomes a way of life** …. In human societies are not generally enforced by constant low-level physical assaults; the backbiting is metaphorical, not literal. But the biological effects may be very similar, leading to the same state of chronic activation of the acute phase response ....

p.203: *Michael Maes* and his colleagues have published evidence that the same chemical messenger that plays a starring role in exporting local inflammation to the brain and triggering the psychological symptoms of the acute phase response after infection — IL-18 — is also produced in greater amounts by macrophages in the blood of severely depressed people.[3] (s.p.53) ….

p.205: The scientific evidence does not back up the claims of *Louise Hay* and other fervent believers in the power of the mind. Cancer is a case in point (cancer is partly the result of mental attitudes; then why shouldn't it be possible to reverse the pathogenic pathway, by reversing abolishing certain mental concepts – reversal of cancer by a mental readjustment. Disease can be regarded as a non-verbal communication pathway of the body; therefore it shouldn't be fought at, but it should tried to understand and reintegrate the aberated physiological process into the coherent bodily system – in the end it is still the same body that brought it to light in the first p[lace) …. The power of the mind to heal the body may not be unlimited, but nor is it negligible ….

Source: Maes, M., Bosmans, E., Vandervorst, C., et al (1991). Depression-related disturbances in mitogen-induced lymphocyte resonses and interleukin-1 beta and soluble interleukin-2 receptor production. Acta Psychiatrica Scandinavia 84: 379-86.

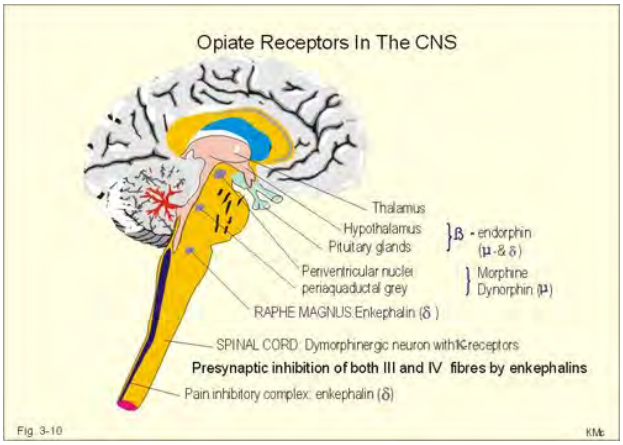
http://www3.interscience.wiley.com/journal/119989884/abstract?CRETRY=1&SRETRY=0

Pain-blocker (4/4)

Endo(genous mo)rphins (EM)

- natural pain relievers (pituitary);
- anti-inflammatory action;
- release via mental activity;
- Naloxone - antidote to EM (trial in dental studio: pain returned, so did the swelling!);

Alem, 1987



Endorphins are endogenous opioid polypeptide compounds. They are produced by the pituitary gland and the hypothalamus in vertebrates during strenuous exercise, excitement, pain, death, and orgasm and they resemble the opiates in their abilities to produce analgesia and a sense of well-being. Endorphins work as "natural pain relievers", whose effects may be enhanced by other medications (wikipedia 2009).

p.57: Naloxone is an antidote to morphine …. Scientists had shown that these receptors were also targets for certain naturally-occurring substances in the brain whose chemical structure was similar to that of morphine …. Even if placebos did reduce pain by triggering the release of endorphins, it was still unclear how and why that should happen in the first place. By what mechanisms could the injection of an inert substance such as salt water send a message to the pituitary gland to release its natural painkillers? And why was the pituitary not releasing them beforehand, when the patient was in such obvious pain?

p.58: Evidence is growing that the power of placebos to reduce pain is due to their ability to unleash the body's own natural painkillers …. In one of these studies the dentists went on to give the patients a dose of naloxone.[15] Just as expected, the pain returned — but so also did the swelling. Naloxone, it seems, does not only abolish the painkilling effect of placebos; it also reverses their anti-inflammatory action. This suggests that the power of placebos to reduce swelling is based on the same mechanism as that which underlies their power to reduce pain - the release of endorphins ….

THE OTHER SIDE OF IMMUNITY

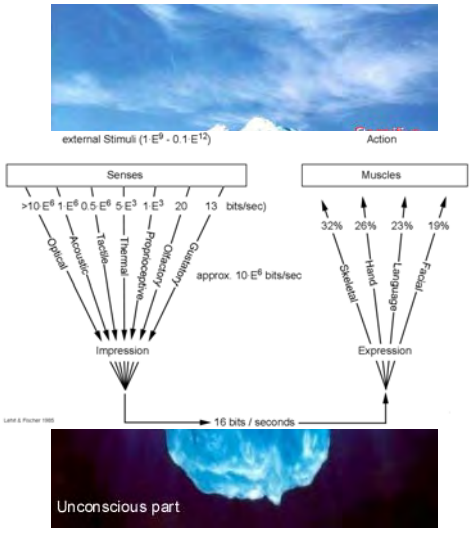
p.59: …. Pain, swelling and fever can all outlive their usefulness, and this indeed is what seems to happen in the chronic inflammatory disorders such as arthritis and, perhaps, depression …. The most important is the distinction between the innate immune system and the acquired immune system. The job of both is to distinguish between self and non-self, but the innate immune system is very ancient, and is found in all animals, including insects and molluscs, whereas the acquired immune system evolved much later and is found only in vertebrates, such as fish, birds and mammals (see *Villarreal*). Unlike the acquired immune system, which can recognise and remember the unique details of each species of bacterium it encounters, the innate immune system works by recognising a few simple characteristics that many bacteria have in common (innate & acquired immune system) …. p.60: In fact, it takes several days before an effective acquired response can be mounted against a particular pathogen, during which time the invading bacterium or virus will have multiplied many times over, gaining ever more of a foothold in the body. The innate immune response, on the other hand, can be activated within minutes of infection, and plays a vital role keeping the invaders at bay until the acquired response can eventually launch its devastating counterattack …. Sometimes, however, for various reasons that remain obscure, the normal control mechanism that turns off the acute phase response malfunctions, and the pain, inflammation and sickness behaviour persist. The acute phase, so to speak, is no longer acute; it has become chronic ….

Source: Alem M.A. (1987): Placebo mechanism in the treatment of post-operative morbidity. Eastman Dental Hospital - University College London;

Me & I (1/5)

Emotion – the limbic cell (Epigenetic Bookmarking)

- newborns "download" huge volumes of information for their personal development
- information programmed into the subconscious mind is defined as "truth" (incl. abuses);
- social world hugely influencing expression of genes (determines neuronal connections);
- generates emotions – via controlled release of regulatory signals (nervous-, endocrine system);
- conscious mind (***I***) reads the flow of cellular signals (which comprises the mind of the body - ***Me***);



Norretranders, 1988

p.131: The evolution of the limbic system …. converted the chemical communication signals into sensations that could be experienced by all of the cells in the community. Our conscious mind experiences these *signals* as emotions. The conscious mind not only "reads" the flow of the cellular coordinating signals that comprise the body's "mind", it can also generate emotions, which are manifest through the controlled release of regulatory signals by the nervous system (unfolding EX-formation) …. *Candace Pert*: …. established that the "mind" was not focused in the head, but was distributed via signal molecules to the whole body (s. also *M.W.Ho*) …. While proper use of consciousness can bring health to an ailing body, inappropriate unconscious control of emotions can easily make a healthy body diseased …. [Pert 1997] ….

p.135: Our responses to environmental stimuli are indeed controlled by perceptions, but not all of our learned perceptions are accurate. Not all snakes are dangerous! Yes, perception "controls" biology, but …. perceptions can be true or false. Therefore, it is more accurate to refer to these perceptions as ***beliefs. Beliefs control biology*!**

p.167: e.g., if a ball flies t/w your eye …. the subconscious mind, which processes some $20 \cdot E^6$ environmental stimuli per second vs. 40 environmental stimuli interpreted by the conscious mind in the same second, will cause the eye to blink [Norretranders 1998] …. Reflex behaviors …. e.g. driving a car at 65km/h on a highway while your conscious mind is fully engaged in conversation with a passenger …. Through the conditioned learning process, neural pathways between eliciting stimuli and behavioral responses become hardwired to ensure a repetitive pattern (**"habits"**) ….

Image: Overview of the information flow through a human being. A so-called organogram. shows that more information goes in and out of humans than consciousness perceives.

According to Hans Kuhn (1988), chemist ….biological evolution consists of a series of choices where an organism relates to its surroundings. These surroundings subject it to pressure, and it must choose to act in order to survive. An organism's genes contain experience in survival – otherwise there would be no organism, and no genes. The more the organism survives, the more it experiences. And the more valuable its genes become. So the interesting thing is not how many genes it has – i.e. how long its DNA is. The interesting thing is the wealth of experience deposited in its genes. The information of organism contains it its genes has a value that is proportional to the mass of experiences compressed there. What's interesting is not the face value of the information – i.e. the size of genes (genome) – but rather the information discarded. "This quality constitutes knowledge, where 'knowledge' is measured by the total number of bits to be discarded". Kuhn wrote. Biological knowledge, then is defined as discarded information. Exinformation is perpendicular to information. Exinformation is about the mental work we do in order to make what we want to say sayable. Exinformation is discarded information, every time we do not actually say but we have in our heads when or before we say anything at all …. Exinformation is the history of the message, information the product of that history – information without exformation is vacuous chatter; exformation without information is not exformation but merely discarded information …. The information in the cohesion of a system cannot be completely localized, since any system is spread over space and time.

Source: Pert, Candace (1997). Molecules of Emotion: The Science Behind Mind-Body Medicine, New York;

Norretranders T. (1998) The User Illusion Cutting Consciousness Down to Size. Penguin Books, NY – USA;

S. Lehrl and B. Fischer (1985). "Der maximale zentrale Informationsfluss" *Grundlagenstudien aus Kybernetik und Geistenswissenschaft / Humankybernetik* 26: 147-154; Lipton B. (2005) Biology of Belief. Elite Books;

Source: Kuhn H, (1988) Origin of Life and Physics: Diversified Microstructure-Inducement to form Information-Carrying and Knowledge-Accumulating Systems. IBM J. Rep. Develop. 32:1 37-46;

Huberman B.A. & Hogg T. (1986) Complexity and Adaptation. Physica 22D: 376-384 …. both quoted in: Norretranders T. (1988) The User Illusion. Penguin Books.

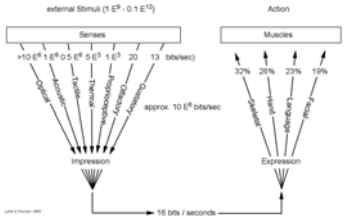
Collier J., Burch M. (1998). Order From Rhythmic Entrainment and the Origin of Levels Through Dissipation. *Symmetry: Culture and Science* Order / Disorder, Proceedings of the Haifa Congress; Vol.9: 2-4;

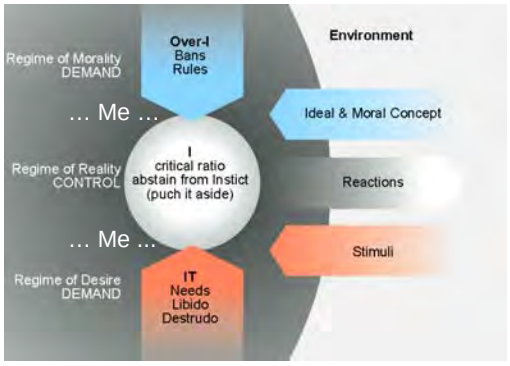
Me & I (2/5)

Emotion – the language of cells

- the "upper-I" (regime of morality);
- the "I" (regime of reality);
- the "IT" (regime of desire);

Liu, 2009





Engaging the subconscious in battle is as pointless as kicking the jukebox in the hope that it will reprogram its play list ….

p.171: Tensions between conscious will power and subconscious programs can result in serious neurological disorders (movie "Shine": why we should not challenge the subconscious) …. Most of us engage in less dramatic battles with our subconscious mind as we try to undo the programming we received as children ….

i) Every decision originates from an emotional and personalized framework; to that is any decision must be emotionally bearable (one must be able to life with it); only on this basis, the intellect (consciousness) comes into effect;

i) Great changes (thinking and behavioral pattern) must evolve on the ground of such an emotional basis;

i) dramatic changes – deep affectiveness – result in fundamental change;

i) an intelectual impulse (e.g. you should not smoke) does not achieve anything; only if the emotinal, deeper spheres are reached can behavioral (=mental) changes be induced;.

Das Über-Ich kann im *Freud*'schen 3-Instanzen-modell vereinfacht als die moralische instanz / gewissen angesehen werden und stellt den gegenspieler für die elementaren lusttriebe des ES dar. Es wird in der frühen kindheit (bis zum 6. LJ) gebildet und enthält die (moralischen) normen und verinnerlichten wertvorstellungen der kulturellen umgebung, in der das individuum aufwächst (insbes. die der eltern!). Das Über-Ich entsteht durch angleichen der eigenen person an andere, mit denen sich dieser mensch identifiziert (introjektion durch die gemeinschaft, gllgemeinheit). Wenn ein mensch zu denken beginnt, geschieht dies bereits unter dem einfluss des Über-Ichs, und der darin enthaltenen grundsätzlichen wertvorstellungen. Das Über-Ich fungiert in der menschlichen psyche als eine kontrollinstanz, deren ziel es ist, durch selbstbeobachtung das eigene verhalten in uebereinstimmung mit dem idealbild zu bringen. Bei ES-bedingten abweichungen von diesem ideal wirkt sich das Über-Ich auf den menschen in form des verspürens von schuldgefühlen aus.

Source: Klussmann R. (2000) Psychotherapie, 3te Auflage. Springer, p.5 & 20-28

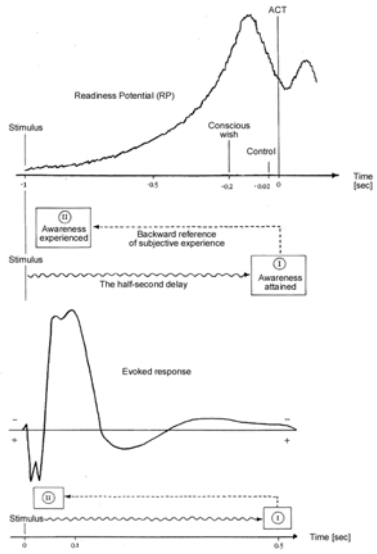
Lipton B. (2005) Biology of Belief. Elite Books

http://en.wikipedia.org/wiki/Id,_ego,_and_super-ego

Me & I (3/5)

Readiness Potential (RP) & Consciousness (C)

- RP of brain starts 0.55s before act;
- Unconsciousness processes are the initiator;
- patient doesn't feel cortex-stimulation if <0.5s;
- If he feels it, backward temporal referral takes place!
- C lags behind – sub-C not;
- C can't initiate an action, but it can veto it;
- **Free will operates through selection, not design;**
- Who makes split-sec's decision?
- Conscious I is just driftwood;
- Not the ***I*** has the power to dispose, it's the ***Me***!



Libet 1983

p.214: The brain displays what Kornhuber and Deecke called a *Bereitschaftspotential,* or readiness potential: a shift in the electrical potential, which shows that an action is being prepared ….

p.218: The readiness potential starts 0.55 second before the act, while consciousness starts 0.20 second before the act.

p.220: Our actions begin unconsciously! **Our consciousness is not the initiator—unconscious processes are**!

p.231: If the cortex was stimulated for less than half a second, the patient felt nothing …. It is only when the cortex has been stimulated for half a second that the feeling becomes a *conscious* sensation. A sensory stimulus leads to a cascade of neuronal activity in the cortex. It is this cascade that leads to a conscious sensation half a second later …. Stimulation of the skin *immediately* results in sensation, but the activity in the cortex required to mediate the sensation has to be at least half a second long .... **Almost half a second** of brain activity is necessary before consciousness appears;

p.232: Consciousness lags behind, but our subjective perception does not lag!

p.235: A subjective relocation in time occurs, and the skin stimulation is consciously experienced as if it occurred at a moment when awareness has not set in but the brain has unconsciously reacted …. The backward temporal referral was proved

p.243: Consciousness has enough time to veto an act before it is carried out …. ***Consciousness cannot initiate an action, but it can decide that it should, not be carried out*** …. **Free will operates through selection, not design** ….

p.245: Morality is a question of what one may *not* do. Again, this means that morality is not a question of what one may feel like doing; morality is a question of what one *does.*

p.249: We notice the non-conscious only when it goes against the conscious …. consciousness is forced to acknowledge that there is more to man than his consciousness are those where there is a **conflict between the conscious and the non-conscious.**

p.256: Can my conscious *I* not determine at all what I get up to? …. We cannot see how we can define an *I* without its involving consciousness. The *I* is characterized by its responsibility and coherence …. The *I* is a spectator to many of its owner's actions.

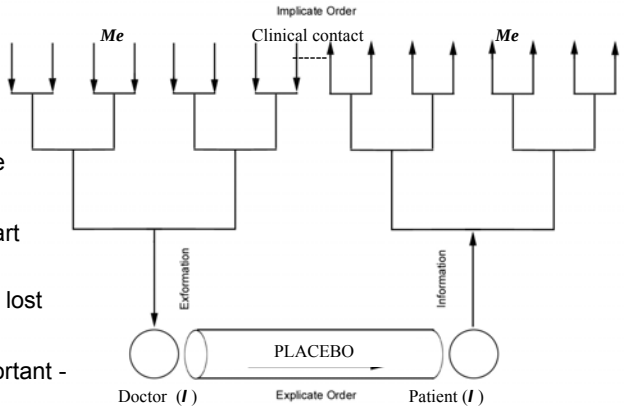
Source: Norretranders T. (1998) The User Illusion; Penguin Books, New York - USA

Libet, Benjamin, Curtis A. Gleason, Elwood W. Wright, and Dennis K. Pearl (1983): Time of Conscious Intention to Act in Relation to Onset of Cerebral Activity- (Readiness-potential). *Brain* 106: 623-42.

Me & I (4/5)

Duality b/w ***Me*** & ***I***

- the ***Me*** is the entire organism; the ***I*** emerges when there's time to think;
- the ***I*** interrupts and confuses, while the ***Me*** is the reservoir of potential;
- the ***I*** must allow the ***Me*** to "**live**" the part …otherwise it triggers disease;
- chronic diseases often involve crises - lost faith in our own abilities;
- type of pharmaceutical often less important - a placebo will usually be as good;
- Its about re-establishing trust b/w ***Me*** & ***I*** ;



Clinical contact b/w doctor and patient (at the high bandwidths) secures the patient-Me's faith in its self-healing abilities. The patient's I *is given a placebo and some medical Latin so the* Me *can be left to heal itself in peace*

Norretranders, 1988

p.108: Whether we do so via phone or face-to-face, our talking time is limited. So what we do is **summarize**: we discard information. **What we call information in everyday life is really more like exformation** ….

p.109: We can give an account of it only when it has "collapsed" (like the wave function) into an event through the discarding of information …. a thing (mess) not structured and organized contains more information, because it is more difficult to describe. We just cannot be bothered to talk about it in detail, so we call it a macrostate, such as heat, a mess, or the dishes to do. Things that contain the most, info are not interest, for they are a mess.

p.111: At the other end, the information is unfolded again. The recipient thinks about the horses she has seen in her life. She associates to experiences, thoughts, memories, dreams, emotions, horses. Excitation takes place.

p.256: Can my conscious *I* not determine at all what I get up to, then? We cannot see how we can define an *I* without its involving consciousness. The *I* is characterized by its responsibility and coherence. The ability to account for its acts and to occasion them is a very considerable part of the idea of an *I*. But the *I* is a spectator to many of its owner's actions ….

p.258: It is not my *I* that has the power to dispose. It is Me ….: I possess free will, *but it is not my* I *that possesses it. It is* Me. We must distinguish between the *I* and the *Me* …. The *Me* is the person in general …. The *I* is in charge of lots and lots of situations where there is time for thought .... The term *Me* embraces the subject of all the bodily actions and mental processes …. The term *I* embraces all the bodily actions and mental processes that are conscious[7]…. In fact, the *I* refuses to acknowledge that there is a *Me* not identical to the *I* itself ….

p.264: Because people mostly convert information in an unconscious way, the conscious *I* cannot automatically activate all the information required for a good performance. The *I* can repeat the text, but that is not enough. The *I* must allow the *Me* to "**live**" the part ….

p.269: The relationship between You and Me thus becomes an internal relationship between *I* and *Me.* Much of the drama that is played out between human beings is really a drama that is played out inside the individual person between the *I* and the *Me.* The *I* represents the social side of things in *Me* ….

p.272: In medical care, for example, it is the general experience of (qualified) doctors that most pharmaceutical are of dubious therapeutic value. The major infectious diseases were eradicated not by pharmaceuticals but by improved hygiene and living conditions. Better diets, housing, and sanitation eliminated diseases such as tuberculosis.[22] But that does not mean that medical treatment does not work. It merely means that it is not necessarily the medicine that works. By far the most effective pharmaceutical known is the ***placebo,*** from the Latin for "I want to please." Placebos work, but not because of the pills or potions prescribed. They are effective because the patient believes they will work ….

p.273: In this context, it is less important which pharmaceuticals are employed, even though for many patients it is vital that a pharmaceutical *be* used. What can happen when such a pharmaceutical is employed is that the *I* again begins to trust the ability of the *Me* to heal itself. Disease often involves crises in which we lose faith in our own abilities: overwork, disappointments, and unhappiness make the body say Stop, and send us to bed with a cold, say …. The *I* does not want to let the *Me* have its way by giving in to the urge to go to bed and eat candy while we watch soap operas and read magazines. The /does not believe in the self-healing powers of the *Me.* So the relationship between treater and treated is really also …. a relationship between the patient's *I* and *Me.*

Image: *The placebo tree. Clinical contact between doctor and patient (at the high bandwidths) secures the patient-Me's faith in its self-healing abilities. The patient's* I *is given a placebo and some medical Latin so the* Me *can be left to heal itself in peace*.

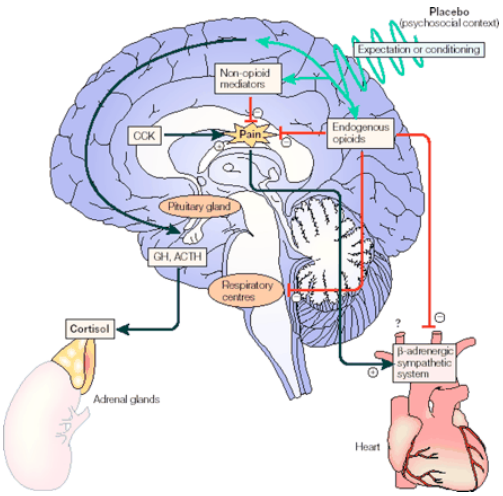
Source; Norretranders T. (1988) The User Illusion. Penguin Books. New York – USA;

Me & I (5/5)

Placebo-Effect

- …. our beliefs act like filters on a camera, changing how we see the world;
- our biology adapts to those beliefs;
- we cannot readily change the codes of our genetic blueprints, but we can change our minds;
- …. a doorstep to epigenetic bookmarking;

Colloca & Benedetti 2005



Henry Ford was right about …. about the power of the mind: "If you believe you can or if you believe you can't ... you're right". Think about the implications of the man who blithely drank the bacteria that medicine had decided caused cholera. Consider the people who walk across coals without getting burned …. Your beliefs act like filters on a camera, changing how you see the world. And your biology adapts to those beliefs …. While we cannot readily change the codes of our genetic blueprints, we can change our minds. You can filter your life …. that turns everything black and makes your body/mind more susceptible to disease. You can five a life of fear and or live a life of love. You have the choice! But I can tell you that if you choose to see a world full of love, your body will respond by growing in health ….

Image: Events that might take place in the brain after placebo administration. Placebo administration (psychosocial context) might reduce pain through opioid and/or non-opioid mechanisms via expectations and/or conditioning mechanisms. The respiratory centers may also be inhibited by endogenous opioids. The {beta}-adrenergic sympathetic system of the heart may also be inhibited during placebo analgesia, although the mechanism is not known (reduction of the pain itself and/or direct action of endogenous opioids). CCK antagonizes the effects of endogenous opioids, thereby reducing the placebo response. Placebos can also act on 5-HT-dependent hormone secretion, on both the pituitary and adrenal glands, thereby mimicking the effect of the analgesic drug sumatriptan. From Colloca and Benedetti (2005).

Source: Lipton B. (2005) Biology of Belief. Elite Books, p.143-144

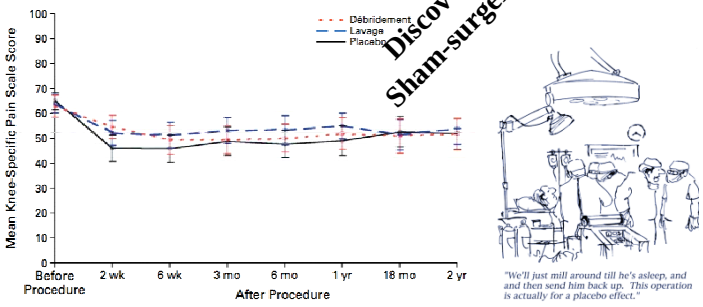
http://www.biology-online.org/user_files/Image/Neurobiology/NE-placeboF01.gif

Sham Surery (1/2)

Sham Surgery

osteoarthritis of the knee recommends:

- arthroscopic lavage (10L of fluids) or
- débridement (washing & shaving of cartilage)
- placebo-treatment: std. arthroscopic débridement procedure was simulated;



Mean values (and 95% CI) on the knee-specific pain scale; higher scores indicate more severe pain.

Moseley et al, 2002

SHAM SURGERY

p.195: If a trial shows that a surgical procedure is no better than a placebo, it can be removed from medical practice, thus sparing thousands of future patients unnecessary operations …. Arthroscopy.[12] …. involves scraping and rinsing the knee joint, is carried out on patients with arthritis in their knees (see dvd – discovery channel) …. Moseley took ten volunteers …. Nobody knew who would get the real operation and who would get the placebo until the volunteers were in the operating theatre and Moseley opened an envelope with secret instructions ….

p.196: Six months later, they still couldn't guess. All reported a significant decrease in pain, and all were happy with their operations. This was only a pilot study — the small number of patients makes it impossible to say for sure that there is really no difference between arthroscopy and placebo — but it was enough to convince Moseley to set up a much bigger study that could provide more definitive conclusions (if this is a placebo effect, then it can't be an acute phase response; can the acute phase response also be observed in chronic events? If so what is then acute – requires redefinition – or maybe acute and chronic are present simultaneously?) …. The patients in the study were divided into three groups. Moseley shaved the damaged cartilage in the knee of one group. For another group, he flushed out the knee joint …. The third group got "fake" surgery. The patient was sedated …. All three groups were prescribed the same postoperative care, which included an exercise program. The **results were shocking** …. The placebo group improved just as much as the other two groups! …. The results were clear to Moseley: "My skill as a surgeon had no benefit on these patients ….

At no point did either of the intervention groups report less pain or better function than the placebo group. For example, mean (±SD) scores on the Knee-Specific Pain Scale (range, 0 to 100, with higher scores indicating more severe pain) were similar in the placebo, lavage, and debridement groups: 48.9±21.9, 54.8±19.8, and 51.7±22.4, respectively, at one year (P=0.14 for the comparison between placebo and lavage; P=0.51 for the comparison between placebo and debridement) and 51.6±23.7, 53.7±23.7, and 51.4± 23.2, respectively, at two years (P=0.64 and P=0.96, respectively). Furthermore, the 95 percent confidence intervals for the differences between the placebo group and the intervention groups exclude any clinically meaningful difference.

Source: www.subtleenergysolutions.com/placebo-cartoon.gif

J. Bruce Moseley, M.D., Kimberly O'Malley, Ph.D., Nancy J. Petersen, Ph.D., Terri J. Menke, Ph.D., Baruch A. Brody, Ph.D., David H. Kuykendall, Ph.D., John C. Hollingsworth, Dr.P.H., Carol M. Ashton, M.D., M.P.H., and Nelda P. Wray, M.D., M.P.H. (2002). A Controlled Trial of Arthroscopic Surgery for Osteoarthritis of the Knee. New England Journal of Medicine. Volume 347 (2):81-88

http://ffh.films.com/id/6611/Placebo_Mind_Over_Medicine.htm

Conclusion (2/2)

…. for chronic situations a ….

- placebo-effect is a necessary by-product of the increasing complexity in higher organisms;
- placebo has an imminent effect on the APR;
- placebo-response denotes a chain of events;
- all sorts of immune activity can be conditioned - incl. activation of Inflammatory responses;
- the ideal placebo differs from person to person - what works for me may not work for you;
- western medicine as a gleaming technological machine may be the essence of a powerful treatment; to a committed practitioner of alternative medicine or to a member of a remote indigenous tribe, other kinds of apparatus may be much more credible;
- placebo's effectively used can substitute expensive and painful surgery.

Danke für Eure Aufmerksamkeit - Thanks for your attention

Conclusion

p.200: …. Ultimately, it is the *belief* in the treatment that sets off the placebo response ….

p.201: Western medicine, a gleaming white machine with lots of buttons may be the essence of a powerful treatment. To a committed practitioner of alternative medicine, however, or to a member of a remote indigenous tribe, other kinds of apparatus may be much more credible ….

p.202: The ideal placebo, therefore, will differ from person to person. What works for me may not work for you ….

p.204: …. placebos work by suppressing the acute phase response, and therefore that they will only help alleviate those medical conditions that involve the activation of the acute phase response. This hypothesis at least has the merit of being fairly lawlike. Yet, as we have seen at several points, the relationship between the acute phase response and various medical conditions is itself a complex thing …. However, treating complex medical situations with placebos, similar beneficial results are obtained when compared to standard surgical procedures ….

Source: Evans D. (2004): PLACEBO - Mind Over Matter in Modern Medicine; Harper Collins Publ.; London - UK