Chapter 5. The immunology of self-deception

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The immunology of self-deception is an important subject. For very good reasons the psychological and immune systems are tightly intertwined. Cause and effect may go in either direction. Repression and disclosure, optimism, meditation, positive emotions and negative, religiosity and the placebo effect—all have important immune correlates. The underlying question is always why. Why should suppression of reality be associated with immune costs and sharing reality, with immune benefits—or why an upbeat personality with immune benefits, and depression with immune costs?

At the outset we should recognize that humans are attacked by an enormous variety of parasites—viruses, bacteria, single-celled protozoa, algae, tapeworms, ringworms, blood-sucking mites, lice, fleas, ticks and so on. Indeed, it is a sobering fact that more than half of all species on earth are parasitic on the other half. Mortality rates from this cause may reach 30% or more per year in birds and mammals among others. Thus, natural selection has organized an incredibly complex internal defense against these attackers, our immune system, a literal "sixth sense", directed inwards to spot invaders and stop them. Some of the invaders turn out to be internal in origin, mutated cells that now proliferate as cancers and must also be treated as invaders and killed.

The immune system is very expensive

The beginning of wisdom about our immune system is to understand that it is energetically extremely costly. It is ongoing, active 24 hours a day 7 days a week. To keep the system running our body produces more than two grapefruit-sized set of cells every two weeks (roughly the maximum life span of many white blood cells). Some immune cells are among the most metabolically active cells in the body. Each of several thousand B cells grinds out ~200 antibodies *per second*. Of course they

can only manage this feat for about a day and a half and must continually be replenished. Because the immune system employs a bewildering array of cell types in a very complex manner, nobody has come close to estimating its metabolic cost—though survival costs of heightened immune activity have been measured in nature in several bird species. Mice lacking an immune system have been created in the lab but these animals are prone to infections of every sort and must be maintained in sterile or near-sterile conditions where they do not particularly thrive.

Short-term responses to immediate parasite attack are typically energetically costly. For every 1 degree C increase in human temperature due to fever, there is about a 15% increase in metabolic rate (roughly, the rate at which we consume energy). Immunizations, which merely mimic parasite attack, commonly elevate metabolic rate by about 15% while real attacks have twice the metabolic cost. This is measured not only in energy but also protein consumed—20% loss in total body protein in sick humans, while in some sick rats >40% of muscle protein is broken down and new synthesis is sharply reduced. Chickens reared in germ-free environments enjoy ~25% gain in body weight compared to those raised in conventional environments. Of course this reflects immune costs as well as costs of the parasites themselves. The metabolic requirements of mammals raised in germ-free environments drops by as much as 30%. Supplying antibiotics in food is associated with growth gains in birds and mammals on the order of 10%.

It is also a striking fact that ~1/10th of all of the proteins produced in our cells are promptly degraded and their peptides recycled--a wasteful process involving largely the lysosome. Some of this involves regulating proteins that are being produced at too high numbers, but the rest consists of grinding up proteins made by viruses, bacteria and cancerous cells in order to recognize and attack them. Thus the immune system is expensive in both energy and proteins. This means also that it is an energy and protein reservoir that can be drawn on for other purposes—and this is key to understanding the meaning of many psychology/immune correlates. Why is our body draining the

immune system of resources when depressed and can we achieve greater energy efficiency by raising our moods?

These trade-offs appear to explain some major hormonal correlates of immune activity. Thus, testosterone suppresses immune function in males in comparison to females and in an individual male's life. Since increases in testosterone are associated with sexual and aggressive opportunities, the body appears in effect to be saying—I will deal with my tapeworm later, right now I'll use some of that immune energy to garner an extra copulation or defeat a rival male. Consistent with this, among young adults, in humans the lowest testosterone males are those living monogamously with children, next higher, monogamously without children, higher still, monogamously with outside sexual activity, and highest of all, those out there, no children, no partner, in full competition. Health maps inversely on testosterone, lifestyles with marriage tending, for example, to increase male lifespan. Work on monkeys, apes and humans show, as expected, that higher testosterone males are more likely to become infected (with such diseases as malaria) and that disease itself lowers testosterone levels—in other words, the body shifts its investment toward the immune system. There is nothing magic about testosterone, by the way, it is only a signal. Some of the same correlations are found in insects, in which testosterone is not involved: males have a weaker immune system than females and suffer higher parasite loads in nature and lower survival, just as in most mammals. This difference is probably general to most animals—certainly males typically suffer higher mortality.

Likewise, corticosteroids—produced in response to stress—are immune suppressors, suggesting that resources are being made available for dealing with whatever is causing the stress and, in any case, for maintenance—even if that temporarily increases risk of disease. (Of course, the effects of prolonged stress are another matter.)

Sickness behavior

One piece of evidence for how expensive (and important) the immune system is comes from "sickness behavior"—the cost that the immune system imposes back on the rest of the body when it needs to repair itself. Right after the immune system has fought off a parasitic invader—let us say a virus or some bacteria—it is literally physiologically exhausted. It has drawn down heavily on its own resources to deal with the invader and it now needs to rebuild itself to be ready for the next one. To do this it induces a state of torpor, apathy, and lack of interest in life in the larger organism—the "blah's". This is achieved by releasing a hormone (cytokine) that acts on the brain to make the person "an-hedonic", that is, not taking pleasure in anything. In rats, this can be shown experimentally by releasing the immune cytokine that targets the brain—the rat simply will not work as hard (on a treadmill) for sugar or other rewards [NAME OF CYTOKINE].

To me this finding was also striking because I had always thought you felt bad after the initial attack of parasites (disease) because you were still fighting them, perhaps mopping up operations but still enough to keep you busy. Now I see that our immune system—fresh from heroic work on the barricades—merely wants to rebuild itself and can we kindly help out by becoming inactive? To redirect energy to itself, the immune system makes other activities unrewarding so that they will no longer be sought out. Internally you experience this as akin to depression. Would we suffer it better if we understood its purpose and went along with the program? Stay in bed, do not try to eat or have sex or pursue other activities that are usually fun—be satisfied with a "vacation from pleasure", preserve your energy and be humble. Things will soon get better.

Sleep is very important for immune function

A profound role for sleep and immune replenishment is emerging from a variety of studies. Totally sleep-deprived rats soon die of systemic bacterial invasions, while

rabbits that sleep more following artificial infection are more likely to survive. Indeed, mammals generally appear to respond to infection with increased sleep. Perhaps the most striking facts come from comparing species of mammals. The more time individuals within a species are able to sleep, the higher are their white blood cell counts for most cell types while red blood cells, which originate from the same tissues but are not part of the immune system, are unaffected. This correlation applies to both REM sleep (with dreaming) and non-REM sleep. Likewise, individuals from species that spend more time asleep are less likely to be infected by parasites—both species and numbers—a strong correlation that holds across a wide range of species. Those with more than 10 extra hours sleep in the sample had rates of parasitism 24-fold lower than those without the extra 10 hours. In short, for long-sleeping species, life may be dull, but it sure is healthy. One important implication is that some of the correlations we describe below for social variables (including disclosure) on immune function may, in fact, be mediated by their effects on sleep. If disclosing trauma to others results in 15 more minutes of less fitful sleep, this alone could induce the immune benefits that have been shown. A striking effect of disclosure is how quickly the benefit kicks in, as would happen if it immediately led to less troubled sleep. We should also note that so-called sleep-deprivation in various torture centers, in Guantanamo and elsewhere, is expected to increase sickness in the victims.

The brain consumes 20% of resting metabolic energy—no matter what

The brain is also a very costly organ. Although only 3% of total body weight, the brain consumes 20% of all resting metabolic energy. When awake, this price seems to be invariant. In the 1950s it was shown that doing arithmetic did not require additional mental energy of the brain, a finding that now seems quaint, given that the 20% energy cost is known to be constant whether you are happy, depressed, schizophrenic or on an LSD trip. The cost is slightly diminished during non-dreaming sleep but slightly elevated during dreaming. Thus throughout the full 24-

hour cycle the brain's resting energetic cost remains virtually constant. Twenty percent is the price of poker in our species—the price to play life with a functioning brain. You must pay it or else. Indeed, not paying it for 5 minutes typically leads to death or, at the least, irreversible brain damage. This is just a fact of life—and an extraordinary one at that.

The invariant cost is important because one might easily imagine that different psychological functions have different energetic costs. Perhaps part of the benefit of depression is that the brain saves energy. No—although the depressed state may lower over-all energy needs, depression appears to have no effect on the 20% of energy the brain extracts. Likewise, if repression (= suppression of truth from the conscious mind) lowers immune function, as it appears to, this is very unlikely to mean that repression itself requires extra energy over and above normal function, the energy being supplied by the immune system. Instead, we must look for other changes associated with repression—which the immune system then pays for.

Genetic activity of the brain and immune system

It has been known for some time that the brain is the most genetically active tissue in the human body, that is, a higher percentage of genes are active in the brain than in any other tissue, almost twice as high as liver and muscle, the nearest competitors. A good 1/3rd of all genes are so called "house keeping" genes useful in running most kinds of cells, so they are widely shared, but the brain is unique both in the total number of genes expressed and in the number that are expressed there and nowhere else. By some estimates 2/3rds of all genes express themselves in the brain, that is ~20,000 genes. This means that genetic variation across humans for mental attributes such as degree of honesty and degree and structure of self-deception is expected to be fine-grained. You may find in life that you repeat the same pattern of self-deception even as you gain limited after-the-fact insight in part because there is a genetic bias that is not easily overcome by experience.

What we do not know is whether there are, as expected, chemicals common to both the brain and immune system such that depletion in one system causes problems in the other. If so, we might expect immune-psychological correlates we would not otherwise see. An analogy may help. In 1982 it was shown that female birds appeared to be choosing brightly colored males as a way of getting parasite-resistant genes for their offspring. This result has been documented many times since then—both that females like brightly colored males and that such males are relatively low in parasite number. It seems to be difficult to be brightly colored and sick at the same time, but why? Only in the 1990s was it shown that carotenoids—which give us our orange, yellows and reds and which are not manufactured by any vertebrate but must come from the diet—play a vital role in immune function. This means that a more active immune system—for example, in response to infection—must draw carotenoids from surrounding tissues to help fight the invaders, as indeed it does. Those that are strong and healthy have color to spare, which they move to the body's exterior as advertisement.

A possible example of the sort I am imagining was first described in the bumblebee. When given a harmless antigen to which the bee mounts a response, the response interferes with associative learning but not perception or discrimination. Since it is unlikely that any of these activities increase the brain's energy budget, one must look elsewhere for an explanation. In honeybees we know that associative learning depends on otopamine, itself a chemical important in their immune system. In vertebrates we know that cytokines produced by the immune system can directly affect the hippocampus and reduce memory consolidation but the functional meaning is obscure. From both humans and abundant experimental evidence in rodents we know that parasitic infection has a dramatic and negative effect on learning abilities, a finding also confirmed for birds. Since the immune system cannot starve the brain of its 20% energy cut, the effect must result because the activated immune system deprives the brain of other chemicals or circumstances vital for learning—perhaps a decrease in REM sleep, now shown to be vital in consolidating learning in various species.

In birds there is clearly an intimate relationship between the immune system and the brain, one that appears to be heightened by the action of sexual selection. Two organs are intimately involved in immune function (mostly B cell production and storage)—the bursa Fabricius of juvenile birds and the spleen of adults. The relative sizes of these two organs are positively correlated with relative brain size across a range of species. This may in part be due to big brains being associated with long lifespan, which places a premium on parasite defense. But the correlation is especially strong when the sexes differ in brain size. That is, the bigger the relative size of the male's brain is compared to the female's, the greater is the relative size of the two key anti-parasite organs in the species. The assumption is that males are especially likely to suffer from parasite load and its associated cognitive impairment (demonstrated numerous times in birds) so that selection, especially in big brained birds, will favor heavier investment in immune functions that will protect especially against cognitive impairment.

It is often not appreciated how much female choice has forced a cognitive burden on males, the better to keep the females entertained. Song repertoire size, which is favored by females, is run in males by a substantial set of neurons in the brain that completely regress during the non-breeding season (clear evidence of the cost of running the show). We would expect pleasing male song to be both sexually arousing in females and immunologically positive.

One striking discovery is that both music and laughter appear to be positively associated with immune benefits. The music experiments were almost too good to be true and were described in the context of religion, where music is often important. Musak, designed to calm people in a claustrophobic situation such as an elevator increased output of an important immune chemical by 14% while jazz did so only by 7%, but no sound had no effect, and noise had a 20% negative effect. Likewise, several studies have shown immune elevation after watching comedies in contrast to neutral material.

Both can be argued to be anti-self-deception. Certainly humor is often directed at drawing attention to the contradictions that deceit and self-deception are hiding. And melodic music may suggest a happy and harmonious structure to the immediate world, while noise is cacophonous and suggests disorder, uncertainty, even danger. Artificially composed monkey (tamarin) music made to match the pitch and tempo of natural monkey sounds but not using the monkey sounds themselves induced behavioral changes in the tamarins similar to what happens in our own species. Tamarin threat vocalization based music induced more anxious activity while affective based music induced less movement, less surveillance, less sociality but more foraging—exactly what you find in other animals when outside threat is reduced. Almost certainly there were parallel immune changes, negative to threat and positive to positive affect, so that the human response to music must have a very long past.

Old-age positivity and immune function

By age 60 if not earlier a striking bias sets in toward positive social perceptions and memories. At ages 20 to 30, we show no tendency to concentrate on faces with positive expressions more often than those with negative ones, later to spend more time examining such pictures nor do we remember them better. In short, we show no bias. But by age 60 a bias appears. When a dot is presented on the side of a screen at which a positive face has just been presented (for one second), the dot is perceived more quickly if it succeeds the positive face and more slowly if it succeeds a negative one. During inspection of faces more eye movement is directed toward ones with positive expressions and they are remembered later more often. This appears to involve a measurable effect in the amygdala where positive faces evoke a stronger response than negative in older people but not in younger ones. Older people, tend to respond to a musically-induced negative mood by preferentially looking at positive faces, as if attempting actively to counter the negative and

maintain or induce a positive mood. Young people tend, if anything, to be mood incongruent—if made to feel bad, they look more at negative faces.

Why show such a positivity bias? Young people will be wise to pay attention to reality—both positive and negative—the better to make the appropriate responses later. To avoid negative information looks risky on its face—negative events may have as big an effect on one's interests (inclusive fitness) as positive ones. By contrast, in old age it hardly matters what you learn—but greater positive affect is associated with stronger immune response, so you may be selected to trade grasp of reality for a boost in dealing with your main problem, that of internal enemies including cancer. A positivity bias sacrifices attention to and learning from negative stimuli the better to enjoy strong immune function now. Grandchildren may admire gramps and grand-ma because nothing seems to faze them, but gramps and grandma are living in positivity land—they scarcely know the difference!

It is an interesting coincidence that although our implicit bias in favor of youth over old age hardly changes with age—from 20 to 70 we favor young over old—by our 40s our explicit bias in favor of youth declines until at exactly 60 we start to say we think older is better than younger. Like everyone else we implicitly associate youth with positive features, but we start preaching the opposite at roughly the same time at which we ourselves display the old-age positivity bias.

Note that the positivity effort requires no suppression of negative information or affect. The bias occurs right away. We simply do not attend to the negative information, do not look at it and do not remember it. Thus, the possible negative immune effects of affect suppression do not need to arise. This must be a general rule—the earlier during information processing that self-deception occurs, the less its downstream immunological effects. At the same time, there may be greater risk of disconnect from reality, since the truth may be minimally stored or not at all.

Writing about trauma improves immune function (and other life outcomes)

In a series of important experiments from the 1980s to the 2000s scientists showed that writing about trauma produced clear immune benefits. Although most of this writing was done in English, the same effect holds true for Spanish, Italian, Dutch and Japanese. In one set of experiments people were asked to imagine the most traumatic event in their lives. They were then split into two groups—those who spent 20 minutes each day for 4 successive days writing in a private diary about their trauma and those who wrote for 20 minutes each day on superficial topics (e.g. what they had done that day). Blood was drawn before the experiment began, after the last day of writing and 6 weeks later. Although those writing on their trauma said they felt worse at the end of the writing than those who wrote on innocuous topics, their immune system already showed an improvement, which was still measurable 6 weeks later, at which time they also reported feeling better (than those who had not written about their traumas). In summary, the immediate feeling of confronting trauma is negative but the immune effects tend to be positive and the longer-term effects on mood and immune system are positive.

What is notable is how little writing is necessary to beget a measurable immune effect some weeks later. A recent review of ~150 studies confirms that there is a general pattern in which emotional disclosure, even in the form of occasional autobiographical writings, may be associated with strong immune benefits. [give examples: hepatitis B, HIV]

One striking effect of disclosure is not on health as such but on the chance of re-employment after losing one's job. Writing about one's feelings after getting laid off appears to be cathartic—people immediately feel better. More striking, at least in one study, is a sharply increased chance of getting a new job. After 6 months, 53% of writers had found a new job but only 18% of non-writers. One effect of writing is that it helps you work through your anger so it is not displaced onto a new, prospective employer nor, indeed, revealed to the employer in any form. This presumably makes you more attractive to them.

Writing about trauma in a private journal in a lab is obviously an evolutionarily recent event but it probably acts as a substitute for sharing this information with others. Certainly rituals of confession are common in most religions, whether public confession as in many New World Amerindian religions or private as in the Catholic confessional. Indeed, the injunction to confess one's sins to God Herself in prayer may serve a similar disclosure function. The benefits of the "talking cure", psychotherapy, may also arise in part from the disclosure of traumatic or shameful information that one is, in fact, hiding from others. When traveling we will often tell secrets to complete strangers, people we have never met before and, crucially, do not expect to see again. The more that people talk in small groups the more they claim to have learned from the group! As one psychologist drily notes, sharing our thoughts is apparently "a supremely enjoyable learning experience". For this reason particular theories of human development—say, Freud's psychosexual stages—may be as valid as astrology yet talking to one's analyst may provide benefits for the same reason that writing in a journal does.

One final feature of the work on expressive writing is worth emphasizing. Computer based analysis has isolated three aspects of the writing that produce beneficial effectsz, emotion words, cognitive words and pronouns. The more people use positive emotion words the more their health improves. Even writing "not happy" is better than writing "sad" perhaps because the focus in the first remains on the positive emotion. Lots of negative emotion words and none at all are both associated with no benefit while a moderate number is. Perhaps one is overwhelmed in the first case and in complete denial in the second. The value in taking alternative perspectives on a problem is suggested by the fact that changing back and forth from the first person (I, me, my) to all other pronouns (they, she, we) is associated with improvement while remaining in one or the other perspective is not.

Conversely there is evidence that inhibition is associated with health problems. Consistent with this, those with undisclosed childhood traumas (sexual, physical or emotional abuse, parental death or divorce) show more illness as adults, including cancer, high blood pressure, flu, headaches and so on. In one study, 10% reported sexual trauma before age 17 and these had the greatest health problems of any group—fewer than ½ had *ever* discussed the problem. From this one might easily imagine that suicide of a spouse would be talked about less than spousal death by other causes and would be expected to be more traumatic. But in fact suicide support groups permit more talking about these kinds of deaths, with better outcomes, a nice example of a cultural invention that permits sufferers to come together to enjoy the benefits of sharing and disclosure.

HIV infection and homosexuality—the effects of denial, disclosure and living in the closet

Given the importance of HIV and AIDS it is hardly surprising that the effects of disclosing or suppressing information have been well studied in those who are infected with HIV, with disease progression itself being taken as a sensitive measure of immune function. The main findings above have been replicated almost exactly. Even relatively modest writing interventions improve apparent health status (immune chemical per viral load). A form of "expressive" group therapy also lowers viral counts while boosting an immune measure. As has been discovered more generally, the writing/disclosure benefits tend only to occur when the writing includes increasing insight/causation and social words. Whether this is cause-and-effect or merely diagnostic is not known.

[add studies with specific effects]

Homosexuality and HIV status also turn out to be especially useful in the study of self-deception because each invites a form of denial that, unlike the experimental

work, occurs almost on a daily basis over a long period of time. Homosexual men often differ in the number of people to whom they reveal their sexual identity (degree to which they are "out of the closet") from only a few non-gay close friends to the whole world. Likewise it is possible to deny HIV+ status to others and to attempt to deny it to self. All of these efforts bring negative immune and health effects and these may be substantial.

Relative to those HIV+ men who are "mostly" or "completely" out of the closet, those who were at least half "in the closet" (or more) enjoyed 40% less time before they suffered from AIDS itself and 20% lower survival rate over-all. Three separate studies show that denying one's HIV+ status to others or even to self ("I am not really sick") is associated with lower immune function and/or more rapid progression of the eventually fatal HIV infection. In HIV+ women evidence of emotional support was not associated with immune change but evidence of psychological inhibition (use of inhibition words in daily speech) was associated—more inhibition, faster immune decay.

It is noteworthy that HIV infection progresses more rapidly in men who hide their homosexual identity than those that openly reveal it. Indeed, the most recent evidence suggests that hiding HIV+ status as well as homosexual identity are both associated with reduced immune function. One study of the progression of HIV in gay men as a function of the degree the men were "in the closet" also controlled for unprotected sex of the dangerous kind (anal receptive). Sure enough, those in the closet practiced more of this kind of sex and this appeared to have a positive effect on the rate at which their HIV progressed (perhaps due to the addition of competing HIV strains). But independently, being in the closet was bad for resistance to HIV. In this respect at least, truth appears to be healthy for the organism expressing it—your immune system is stronger and at the same time you are more conscious—in this case, less likely to act in obviously self-destructive ways. The U.S. government's policy on service by homosexuals "don't ask, don't tell" turns out to be an

immunological disaster. You are asked to deny your sexual identity, which will invite a host of unwanted and unnecessary immune problems for you, all in order to keep everyone else relaxed! [Blacks and Hispanics heavily over-represented: AM]

The ill effects of concealing one's homosexual orientation are not limited to HIV+ men. In a sample of 22 HIV- gay men studied for 5 years, those who concealed their homosexual identity were ~2 times as likely to suffer cancer and infectious diseases such as bronchitis and sinusitis than those who did not. These results are independent of a variety of potentially confounding factors such as age, socio-economic status, drug use, exercise, anxiety, depression and so on. What is especially striking is that for both cancer and infectious diseases the effect is strictly dose-dependent—the more you are in the closet, the worse for you.

There is a very interesting interaction between how rejection-sensitive you are as a homosexual man and the degree to which being in the closet is harmful to you immunologically. Those who are more rejection sensitive are more likely to remain in the closet—where they avoid rejection and benefit from this. Apparently there is a general cost to remaining in the closet but a variable benefit when one is rejection sensitive such that the benefit can overwhelm the cost. Recent evidence suggests that there may be cardiovascular correlates of disclosing homosexual orientation as well.

Positive affect and immune function

There is now abundant evidence that degree of positive affect—whether as a regular trait or only a temporarily induced state—is positively associated with immune function. You feel better you perform better. Here positive affect refers to pleasurable engagement with the world as reflected by such feelings as happiness, joy, excitement, enthusiasm and/or contentment. Related concepts are self-esteem, optimism, extraversion and mastery. These variables are often measured through

self-reports, for example, adjective check lists. Positive affective states are induced for short periods of times, minutes, hours, less than a day, by such devices as listening to positive music, watching positive films, imagining positive states or adopting positive facial expressions (smiling). Self-report measures using checklists of positive and negative terms can be used to measure either short-term states or longer-term traits (lasting more than one week). In general, the evidence is stronger, as expected, for a positive immune effect from longer-lasting positive traits than from temporarily induced positive states.

Another line of evidence comes from a study of the two hemispheres of the brain. They often differ at least slightly in their degree of electrical activation. For right-handed people, greater left-activation (as measured by the EEG) is associated with greater positive affect and, in turn, greater immune response to a novel vaccine 6 months later. The converse is true for the right hemisphere. The key is the definition of positive and negative, namely, approach and avoidance. Approach emotions (including aggression) map on the left (positive) side and are associated with immune strength while withdrawal (and anxiety and depression) are associated with right brain activity and a weaker immune response. Why is withdrawal more costly than advance or at least associated more with the need to maintain energy resources?

It is noteworthy that several weeks of so-called "mindful meditation" shift individuals toward greater left brain activity, more positive affect and a stronger immune response. (Whether it also affects testosterone or cortisol levels is unknown.) This demonstrates once again that we are capable of manipulating our own immune system by manipulating internal mood and that these effects may last several months.

Studies of the effects of induced temporary moods (~15 minutes) show similar positive effects on immune function (as measured by secretory Immunoglobin A,

sIgA, in saliva) of both positive and negative mood. This antibody provides the main immunological defense of mucosal surfaces against viral and bacterial infections. It may be elevated under stress and other negative emotions in response to perceived danger of infection or need of wound healing. Yet studies of natural variation in daily mood across a 10 week period show higher sIgA on days of higher positive mood relative to lower and lower sIgA on days with greater negative mood relative to less.

Direct experimental test confirms a strong association between positive affect and immune function but are unclear regarding the correlates of negative affect. Challenging people who have never been exposed to hepatitis B with a hepatitis B vaccine shows a clear positive association between positive affect and a strong, positive immune response, no matter whether the measure of positive affect emphasizes calm, well-being or vigor. Although negative affect has the opposite effect, this was not significant when corrected for positive affect. In general, it seems as if positive affect is not merely the absence of negative and vice-versa, in some cases they act as independent and in others as partly independent variables.

Measures of positive affect are also associated with better survival in relatively healthy elderly who are living free in their communities, while, if anything, positive affect is associated with reduced survival among those already institutionalized. Likewise, those with terminal conditions such as malignant melanoma and metastatic breast cancer are worse off with positive affect but in diseases with higher long-term survival, such as AIDS and non-metastatic breast cancer positive affect is beneficial. It would be very interesting to have a functional explanation for this anomaly.

All of this work is consistent with an immunological theory of human happiness in which a finely tuned immune system purring along at near-peak efficiency with hardly a target in sight would be experienced internally as a highly enjoyable state.

Even such variables as absence of food (hunger) or water (thirst) must be at least partly aversive because of their negative effects on the immune system. At the very least it must be true that as the brain looks outward and acts to increase inclusive fitness in part by increasing "happiness" then surely the same must be true when looking inwardly.

According to this view, the brain is split between outward-directed and inward-directed activity. In the outside world many features are stationary and predictable—the shape of your bedroom, the location of food in your refrigerator, the way to work, etc. Within this world of course there is important variation, a predator appears, a food source, a possible mating opportunity, a hole in the street, to all of which you are selected to make appropriate responses. You have an internal reward/punishment system that goads you in appropriate directions.

Now imagine the whole thing all over for the internal system. Your brain looks inward and sees many constant features—feet and hands further from it than the trunk, a particular circulatory system through which almost all chemicals must ultimately pass, including those produced by the brain to regulate downstream chemical activity. But in this world also live in principle hundreds and even thousands of species of parasites, at the moment just a few perhaps but taking particular configurations that need to be countered. The brain may receive or note signals that a major infection is underway in the lower left abdomen but miss the fact that a core of parasitic cells reside in the right big toe, capable of regenerating the primary attack.

One important distinction concerns consciousness. We are highly conscious of interactions outside our bodies but highly unconscious of interactions within the body. Why? Part of it is that many signals to self need no consciousness but one wonders why we are so unconscious of parasitic interactions—for example failing to appreciate the meaning of "sickness behavior".

Despite its importance, almost no attention has been directed to measuring the correlates of immune function with such major components of individual fitness—or reproductive success—as survival, fecundity, physical attractiveness, and so on. The comparative work has all been done in birds. Here the pattern is clear. A greater natural immune response to some kind of challenge is positively associated with survival in nature and the lab and the effect size is relatively large—18% of variation in survival is explained by immune variation, while the closest competitor, degree of bodily symmetry, explains only 6% of variance in survival.

The placebo: immune effects?

The placebo effect refers to the fact that a chemically inert or innocuous substance administered as if it were a medicine often produces beneficial—even medicinal—effects. This effect is so consistent and strong that all medical trials routinely have a placebo control. That is, if you are giving a pill to test whether it helps people with arthritis, you must give an equal number of people a similar-looking pill lacking the key chemical, and consisting of sugar or calcium or whatever. Only if your medicine works better than the placebo can it be said to have any effect of its own. Of course it would be nice to add a third category to the analysis—no placebo, no medicine—to measure more precisely the placebo effect but doctors have been slow to catch on to the need for this.

The placebo effect is stronger

the larger the pill,

the more expensive it is,

capsule better than pill,

the more invasive the procedure (injection better than pill, sham surgery is good),

the more the patient is active (rubbing in the medicine),

the more it has side-effects, and

the more the "doctor" looks like one (white lab with stethoscope).

The color of pills affects their effectiveness in different situations: white for pain (through association with aspirin?), red, orange and yellow for stimulation, and blue and green for tranquilizers. Indeed, blue placebos can increase sleep via the blueness alone with probable immediate immune benefits.

But the general rules are consistent with cognitive dissonance theory—the more a person commits to a position, the more he or she needs to rationalize the commitment and greater rationalization apparently produces greater effects. Surgery offers repeated examples of placebo effects. One of the great classics is the case of angina (heart pain) treated surgically in the U.S. in the 1960s by a minor chest operation in which two arteries near the heart were fused in such a way so as (allegedly) to increase blood flow to the heart, thereby reducing pain. It did the trick—pain was reduced, patients were happy—and so were the surgeons. Then some scientists did a nice study. They subjected a series of people to the same operation, opening the chest, cutting near the arteries, but they did not join any arteries. Everyone was sewn up the same way and nobody knew who had received which "operation" when later effects were evaluated. The beneficial effects were identical to those of the original operation—in other words, the entire effect appears only to be a placebo effect. The joining of the two arteries has nothing to do with any beneficial effect!

Surgery appears to be unusually prone to placebo effects—presumably because of the great cost and the apparent massing of group support. In any case, most interventions are dubious in advance and with potential for future complications—to be corrected by further surgery—think Michael Jackson's face. So there are built-in incentives for an entire sub-discipline to develop in unhealthy ways. Remunerectomies are an example—operations performed solely to remove a patient's wallet. Consider arthoscopic surgery, meant to correct defects in the knee, for example, due to osteo-arthritis. A very small study suggested that sham

operations—with all the features of real ones—produced virtually the same benefits as the actual operations, suggesting that those were mainly beneficial as placebos. The actual operations were associated with greater maximum pain than the placebos, presumably because they were more inasive, but for over-all level of pain and other measures, the placebo and surgery produce remarkably similar effects.

For effects on pain the placebo has been studied in some detail and there is no question that in some individuals, the mere belief that a pain reliever has been received is sufficient to induce the production of endorphins that, in turn, reduce the sensation of pain. That is, what the brain expects to happen in the near future affects its physiological state. It anticipates and you can gain the benefit of that anticipation. The tendency of Altheimer's patients not to experience placebo effects may be related to this inability to anticipate the future.

Expectancy can create strong placebo effects through a mixture of past experiences of genuine medical effects mixed with placebos. As one author has put it:

> The medical treatment that people receive can be likened to conditioning trials. The doctor's white coat, the voice of a caring person, the smell of a hospital or a practice, the prick of a syringe or the swallowing of a pill have all acquired a specific meaning through previous experience, leading to an expectation of pain relief.

Depression seems especially sensitive to placebo effects. Numerous studies have made it clear that genuine "anti-depressants" account for about 25% of the improvement while the placebo effect accounts for the remaining 75%. Believing you are getting something to help you is more than half the battle. I always think about this when I am being given an anti-depressant. I am told not to wait for an effect for at least 3 or 4 weeks—"it needs to build up". In other words, expect no direct test of utility any time soon and the usual rule of regression to the mean—or, things get better after they have gotten worse—will give you all the evidence you later need. In the meantime, get with the program!

The ability to produce auto-stimulatory effects is nicely illustrated by work on female sexuality. Women who appear to be sexually dysfunctional in failing to respond orgasmically can be induced to greater arousal by giving them false feedback on the bloodflow to their pelvix, itself a correlate of arousal. They appear to be talking themselves into greater arousal, somewhat like the sight of a man's own erection increasing his sexual desire.

There is no doubt that placebo effects operate in athletics as well. Trials have shown that cyclists respond positively to word they have been given caffeine (without getting any) about half as well as to the caffeine itself (along with word they are getting it). Merely telling the cyclists they are getting a heavier dose of caffeine produces a stronger positive athletic response. Even that cliché of working out—no pain no gain—has a built-in placebo-effect.

The analogy with religion is strong and tempting. Both involve strong belief. Both involve a series of conditioned associations including common "doctor or pastoral" elements. And, indeed, until very recently (~5000 years max) medicine and religion were one. One can easily imagine that regular religious attendance (especially if the music is good!) would intensify placebo and other immune benefits, just as regular visits to a caring and sensible doctor or advisor might.

A striking feature of placebo effects is that they are highly variable across a population. Typically roughly 1/3rd show very strong effects, perhaps 1/3rd moderate and 1/3rd none. This is a striking example of what we have emphasized repeatedly, that the deceit and self-deception system must be an evolving one, with important genetic variation for forms and degree of deceit and self-deception. We do not know how much the variation just mentioned is genetic but recent work shows that people with depressive disorders differ in the degree to which they show a placebo effect based on particular genes they do or do not possess. What else

correlates with tendency to enjoy a placebo effect? For one thing, suggestibility, as in ease of being hypnotized, a trait that also shows high variability, some people being highly resistant and others easily manipulated.