Human robustness and conscious purpose in contemporary medicine

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Abstract

Purpose – The purpose of this paper is to ask what role robustness plays in current medicine and in how far medical practices influence human robustness and thus the ability to be adapted and survive under changing conditions.

Design/methodology/approach – In order to do this Bateson's concepts of learning and network pathologies are applied to the medical topic of immune reaction.

Findings – Current medical research does not take sufficiently into account that natural stimuli and therapeutic interventions might lead to a large-scale of changes. This is mainly due to the lack of related epistemological tools.

Practical implications – This lack leads to a restricted validity of many medical findings. There is even some evidence that the current therapeutic approach might lead to a decline of human robustness.

Originality/value – This paper shows how systemic concepts can contribute to a deeper understanding of the therapeutic processes.

Keywords Learning, Adaptability

Paper type Conceptual paper

Robustness

Between August 4 and 18, 2003 about 15,000 people died during a heat wave in France and in the winter 2003/2004 about 50,000 people died in the UK of the consequences of cold weather, over 2,500 in one week. At least in France this was no harvesting effect (people who were expected to die within the next months), but a clear excess mortality (Poumadère *et al.*, 2005).

It is quite safe to state that a lot of people had a reduced ability to adapt to changing weather conditions. Although the weather was quite extraordinary (the summer 2003 was hotter than the last 50 years), the conditions cannot be regarded as extreme. These conditions might even represent the normal case when the predictions of meteorologists become true and summers become hotter due to the greenhouse effect and/or winters colder due to the reduced circulation of the Gulf stream.

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In the first place these people did not die because they were not sufficiently adapted. This would be a mere tautology. It is also inappropriate to say (as often read) that they died because of hyperthermia and heat stroke (summer) or bronchitis or coronary thrombosis (winter). These are descriptions of how they died but do not refer to causes. In general, the question of a cause is problematic as it involves certain silent assumptions. There is always a danger to use a kind of logic which, in its final consequence, leads to ridiculous results such as "people died because they were alive". The statement that people died because of dehydratation involves a simple measure (drinking) which improves adaptation during hot periods. The statement that people died because of a lack of fuel due to poverty (Rudge and Gilchrist, 2005) introduces a political point of view. If people had more fuel they would not have died. But many important questions remain. Why did more people die during the cold in Britain than in Russia where the weather is colder, people are poorer and medical treatment less available? And why did relatively more people die in France than in Portugal where weather conditions were not much different? Is it simply the fact that the Portuguese and Russian people are more used to such kind of weather? And what would this imply?

Such questions cannot be formalized easily in medicine. Our attempt is to use some of Bateson's logical tools, in order to open new ways of thinking and to tackle this and similar problems on a sound basis. First, we prefer the term robustness instead of adaptation. Robustness is clearly defined as the stability and evolvability of a system towards perturbations and under changing conditions (Ahn *et al.*, 2006). It became a well-known notion lately and refers more to the point of view of the physician than adaptation. Moreover, robustness has already a long tradition in medicine. In balneology robustness was and is increased by a procedure called hardening (including cold baths, warm applications, physical exercise, etc.). As a matter of fact, hardening increases robustness not only towards a defined stressor, towards warm (Sauna) or cold (cold baths). Health in general is improved. This is not only the old knowledge of balneologists and proved by hundreds of observational studies. The effects can also be demonstrated on the level of lymphocyte reaction (Kreutzfeldt *et al.*, 2003).

But in the current medical discourse robustness is rarely taken into account. The propositions made to reduce mortality due to extraordinary weather conditions, for example, mainly involve technical interventions such as heating or cooling. For example, a proposition was made to heat the waiting areas of public transport in Britain during winter (Keating and Donaldson, 2004). Such a measure might prove to be effective in an observational study. However, it would be quite expensive and promote climate change even further. That is, both consequences of such a move (the lack of money and climate change) might lead to a further increase of mortality in other areas. Furthermore, such a measure does not improve the robustness of the people to cold weather conditions. It even might reduce it as it represents a kind of "weakening". Bleuler who never heated the floors in his hospital and also kept the ward rooms on a quite low temperature, maintained that he had no deaths during the Spanish flu 1918/1919 whereas comparable institutions had quite a lot of casualties. He insisted that providing a frame of good healthy conditions is the best way to prevent and treat most of the diseases (Bleuler, 1962, pp. 54-6). As the danger of an epidemic of an avian flu is imminent, his arguments are as relevant as 80 years ago. Today the discussion on prevention centres only around drugs and vaccination, well knowing

that in an epidemic both will not be sufficiently available and may even not be effective. We attribute the lack of an understanding of robustness to the fact that the currently used epistemology is not appropriate to describe such phenomena.

Current medical epistemology and its limits

The current medical paradigm is characterized by two main features: first, modern medicine is based on measurement. By that observations are quantified and experiments become comparable. Second, in order to cope with the complexity of human physiology and pathology the observed phenomena are broken down into defined parts, a procedure called reductionism.

Under the conditions of such an experimental setting a certain range of observation is defined. In this range parameters and their changes through interventions can be coherently tracked. Thus, the concept of cause and effect is introduced.

The received descriptions and reactional patterns (physiology, pathology, biochemistry, etc.) are called specific. Current medicine speaks of "specific" diseases like rheumatoid arthritis, mononucleosis or diabetes mellitus. Interventions to alter such specific pathologies are called "specific treatments". Methotrexat in rheumatoid arthritis, insulin in diabetes or neurotransmitters in depression represent such treatments.

Bateson called this specific approach conscious purpose. This expression refers to an attitude where in a complex ecological context certain defined goals are aimed at with defined interventions (Bateson, 1972, pp. 426-47). Conscious purpose in the reductionist setting implies that internal and recursive reactions of the organism are not taken into account. That leads to a situation where the scientist uses epistemological tools that do not really fit for natural processes. That is, the construction of the specific/unspecific frame does not represent a final truth, but the condition of the observer by allowing only certain observations and excluding others. But the predictability of the specific approach is limited as a lot happens outside the defined frame of observation. These events are necessarily qualified as unspecific. There are side effects which are called unspecific, when they are not predictable by the physiological model. There are unspecific diseases with no clear-cut pathology. Chronic fatigue syndrome is such an example, despite many attempts to formulate a specific nature. And of course, there are unspecific therapies. The placebo effect is one. Hardening is another.

In regard to adaptation the specific approach creates problems:

- In reductionism the effect of an intervention or of a therapy has to be based on certain criteria (surrogate-parameters). But such parameters might not be relevant for robustness and there is always an insecurity whether the defined space of observation and the chosen parameters are relevant. If not, an intervention might show outstanding results but might lead to a decline of robustness. Around 1980-1990 the standard therapy of osteoporosis (defined as the loss of bone mass) was sodium fluoride (NaF), known to stimulate osteoblasts. According to all (mostly industry sponsored) trials the therapy was effective. It took years and an independent study to show that, in fact, bone mass was higher but so was the incidence of extra vertebral fractures. Through the therapy bone mass had increased, but the bone had become more brittle (Riggs *et al.*, 1990).

- As reductionist research needs defined conditions the validity of its findings is restricted when conditions change. That is, something effective in a certain context might turn out to be ineffective or harmful in a different context. For example, β receptor blockers are helpful in a lot of diseases from hypertension over glaucoma to anxiety. One of its adverse reactions is that it reduces reactability during hot weather conditions, thus increasing heat-related mortality (Bouchama and Knochel, 2002). Thus, under changing conditions – such as climate change – former evidence might loose its validity.
- The effects of a therapy might exceed its "conscious purpose". For example, there had been reports that the vaccination of children in Guinea Bissau led to an increased overall mortality (Kristensen *et al.*, 2000). Another study showed that the vaccination with DPT and BCG in Burkina Faso led to a decrease in overall mortality (Vaugelade *et al.*, 2004). These effects could be neither explained by statistics nor by the specific reaction towards tuberculosis, diphtheria, tetanus or polio. Although highly specific such findings are normally labelled as unspecific (Fine, 2004).

The concept of learning in the medical context

A suitable epistemological tool to model such effects is the concept of "learning of higher order" introduced by Gregory Bateson. He distinguished five types of learning (Bateson, 1972, pp. 159-76, 279-308):

(1) *Zero learning* is found in cases where an "entity shows minimal change in its response to a repeated item of sensory input". This is seen in simple mechanical circuits or in living organisms which are overstimulated, or where the response is structurally fixed.

(2) *Learning I* is the typical learning investigated in laboratories. It measures to which extent and in which time a person is able to solve a mathematical riddle or to remember nonsense syllables. Learning a language is also learning I.

(3) *Learning II*, or *deutero-learning* is a second order phenomenon. It is learning to learn. Someone who learns nonsense syllables is after a few tests able to learn nonsense syllables more easily, or might even remember numbers better. Learning a language enables an individual as well to learn a different language more easily. But second order learning cannot be detected by the simple measurement of a certain variable. It can only be detected by series of similar experiments and their comparison and a related theory.

(4) *Learning III* is characterized by more fundamental changes. It involves learning to limit, direct or change what is aquired by learning II. We propose as a paradigm the change from a reductionist and linear approach to an ecological/systemic thinking. Such a change does not involve measurements or comparison of measurements. It is a different understanding of data and contexts altogether.

(5) *Learning IV*, according to Bateson, is a change in the learning structure, that is, a change of the genetical adaptation which only happens due to evolutionary selection involving many generations.

During his lifetime Bateson changed this concept several times (Lutterer, 2000, pp. 123-40). One reason might have been that there are some difficulties in its application to observations. There are no major problems with learning 0-II. There is, however, some

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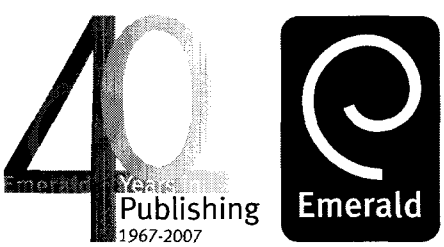

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incertitude about what learning III really is. But the main obstacle is learning IV. Bateson's concept is based on the old axiom that transmission is the transmission of DNA and that acquired characteristics cannot be transmitted. Yet, during the last years epigenetics (the science which investigates how heritable changes occur without a change in DNA sequence) is flourishing and it becomes quite doubtful what "inheritance" really means (Jabolka and Lamb, 2005).

The knowledge on epigenetics is still quite rudimentary. But it is clear that single nutrients, toxins, behaviours or environmental exposures of any sort can silence or activate a gene without altering its code. That is, a given genotype can give rise to different phenotypes depending on environmental conditions. Such responses to the environment may be expressed in the offspring rather than in the parent and might persist across a number of generations, even if the environmental factor itself has changed (Bateson *et al.*, 2004). The following examples shall just give an impression of what is attributed to epigenetics today:

- The nutritional status of grandfathers before adolescence has been found to be of major influence for the health of their grandchildren. A period of famine, for example has a health protective influence in the grandchildren (Kaati *et al.*, 2002).
- Good baby care in rats activates some genes in the hippocampus. This activation remains for generations and these rats show more care for their babies (Weaver *et al.*, 2004).
- Genetically similar fish have different gene expressions according to their life-style and genetically different fish have a similar gene expression when they share the same way of living (Giger *et al.*, 2006).
- Environmental stress changes plant physiology over generations (Molinier *et al.*, 2006).

Although we do not believe that different levels of learning really exist (we regard them as a metaphor), they are helpful in sorting out different aspects of a certain reaction, aspects which are often not taken into account in the judgment of an intervention. Such categories are necessary when the restricted point of view of a linear model is left behind. This shall be demonstrated with the example of immune reaction.

Learning 0 prevails when under similar circumstances a certain infection reoccurs. Some people develop tonsillitis having a cold, some women suffer from herpes labiales during every menses. Also short-term death after an infection should be regarded as learning 0.

Learning 1 is, for example, the development of a lifelong immunity after an infection as in measles or varicella.

Learning II is observed when the immune reaction triggered by one germ improves the immune reaction against other germs. In AIDS there is a survival benefit when the person is infected with the GB virus, a close relative of the hepatitis C virus (Pomerantz and Nunnari, 2004), or with measles (Moss *et al.*, 2002). To go through a flu might improve robustness towards bacterial infections.

Learning III occurs when an acute infection is the starting point of the improvement of a chronic disease. A classical example are worm infections improving asthma (Wilson *et al.*, 2005) or Crohn's disease (Summers *et al.*, 2005). That is, the impact of

an infection onto the immune system might have a beneficial effect for the function in general and is not limited to the protection against germs. This example of learning III is also the core of the so-called hygiene hypothesis (Watts, 2004). This hypothesis says that the exposition to germs is beneficial, as children who live in an environment with a lot of germs (on a farm or with many siblings) are less likely to develop allergies, asthma and many other diseases.

Learning IV is given when following generations benefit from an infection of their ancestors. When measles, varicella and other viral diseases came to the new world through the Spaniards, they were extremely lethal during the first decades. The same was true for syphilis which – according to the prevailing theory – was brought back by Columbus in return. But after some time the diseases became less aggressive. Even people who never had contact with the germ before and probably did not possess specific antibodies had milder forms. Former theories explained this only by selection. It was supposed that the more susceptible people just died, so that the surviving population became genetically more resistant. However, this theory was never convincing. It is not probable either that all germs change when they remain in a new population. This typical example of learning IV involves certainly a strong epigenetic component.

But the ecological context plays a role, too. As seen in learning II the "infection" with certain viruses might lead to a survival benefit in other viral diseases and a person equipped with a certain set of viruses might be better adapted when confronted with a new virus. That is, a person defined as more or less ill in a certain context might be better adapted in the case of an epidemic. One reason is that the immune system normally overreacts when confronted with a totally new virus. For example, the high mortality of Spanish flu 1918/1919 was due to such an overreaction and not to the lack of immune response (Kobasa *et al.*, 2004).

It would, however, be a mistake to believe that learning through germ contact only induces positive effects. An infection often has severe side effects like glomerulonephritis after a streptococcal tonsillitis (learning I). An infection might promote or worsen other infections (learning II). Infections might lead to a total change of human function (learning III). This is seen in many chronic diseases and lately a whole range of such chronic diseases are attributed to infections. This so-called germ theory (Edwards, 2002) is actually the opposite of the hygiene hypothesis. And all this might have negative influences onto following generations (learning IV).

This analysis shows that in the living organism the observation of only one factor (the effect of a "conscious purpose") is necessarily defective. An intervention might produce favourable results but might lead to the decline of robustness simultaneously.

Although this can be partly modelled with the levels of learning, poly-contextual models (von Goldammer and Paul, 2007) or the concept of network pathologies are necessary to understand deeper impacts of a certain stimulus.

Network pathologies

A network pathology arises when the feedback mechanisms of the organism are no longer tuned and the response to perturbations becomes inadequate.

The tuned immune reaction depends on the balance of two types of helper cells (Th). An overweight of Th 1 cells (cell mediated immune reaction) leads to autoimmune diseases like multiple sclerosis (type 1 diseases). An overweight of Th 2 cells (humoral immune reaction) is associated with atopic disease, asthma and other (type 2 diseases)

(Kreutzfeldt and Müller, 2001). In rheumatic disease, for example, the same genetical disposition might lead to the type 1 disease of rheumatoid arthritis (Tokuhiro *et al.*, 2003) or to the type 2 disease of lupus erythematosus (Prokunina *et al.*, 2003).

It became recently clear that the adequate immune reaction is a tightrope walk between autoagression (type 1) and inappropriate defence (type 2). Little is known how the balance is kept. But infections certainly play a central role in the development of an equilibrium and in its loss. It is somehow striking that the two types of helper cells inhibit each other through a negative feedback mechanism (Park *et al.*, 2004). Without outer influence they tend to develop a schismogenetic pattern. But as not every disturbance of the Th1/Th2 relation leads to a chronic disease (many diseases show up in mild form for some time and occur never again) this antagonistic organization has to be embedded in a wider semantic structure with other positive and negative feedback mechanisms involved. That is, the cause of the chronic disease is neither found in Th1, nor in Th2, nor in the relation of Th1 and Th2 alone.

One of the first to study how network pathologies evolve was Bateson. He distinguished two types of pathologies (Bateson and Bateson, 1988, p. 119):

(1) monotone change, continuous increase or decrease; and

(2) to fix a value of a variable.

A pathology of the first type (monotone change) is seen when the negative feedback mechanism between Th1 and Th2 is not interrupted. Experience tells us that it takes months or even years until chronic diseases arise after the occurrence of the first symptoms. Much quicker is the development in Systemic Inflammatory Response Syndrome (SIRS). An inflammatory cascade might lead to sepsis within hours or days.

The second network pathology (fixing a variable) is more difficult to conceive. Bateson starts with the premise that all biological systems contain subsystems which are potentially regenerative, that is, they would go into exponential "runaway" if uncorrected. These regenerative potentialities depend on other subsystems to which they are connected through cybernetic feedback loops. If in such a system, due to outer influences, one variable is held constant other variables are necessarily changed. After some time such a change will spread through the whole system leading to a different homeostasis. He defines such a change as a kind of learning (Bateson, 1972, pp. 440-7). As a consequence, of this change unexpected runaways will occur after some time (Bateson, 1972, pp. 330-1).

This hypothesis implies that modern medicine which often aims at holding variables stable tends to induce network pathologies. As so often in medicine, such a hypothesis would be difficult to prove. An example in this direction is the analysis of polytraumatised soldiers of the battles of Trafalgar and Waterloo. It revealed that the survival rate was then about the same as in today's intensive care, despite all drugs and technology. The main reason why current intensive care does not prove better is the high incidence of sepsis (Singer, 2004), the typical example of a runaway. As sepsis became one of the leading causes of death in the Western world it might be concluded that runaways through the fixation of a variable occur mainly (or become more visible) under extreme circumstances.

The related picture of cybernetics is that of the tightrope walker. A tightrope walker makes chaotic and sometimes vehement movements with his bar in order to keep his balance. Inhibiting his free movement facilitates his falling.

There is growing evidence that this simplistic picture is quite meaningful for human physiology. In all kinds of processes a chaotic distribution of variables is an expression of health, whereas constancy is an expression of disease.

In Figure 1 the course of calcium concentration in blood (above), of parathormone (middle) and its metabolite amino acid (below) is intense and chaotic in the healthy (a), with a loss of nearly all oscillation in severe osteoporosis (b) (Gerok, 1990, p. 30).

Figure 2 shows the analysis of heart rates (PhysioNet). A and C derive from patients in sinus rhythm with severe congestive heart failure. D is from a subject with a cardiac

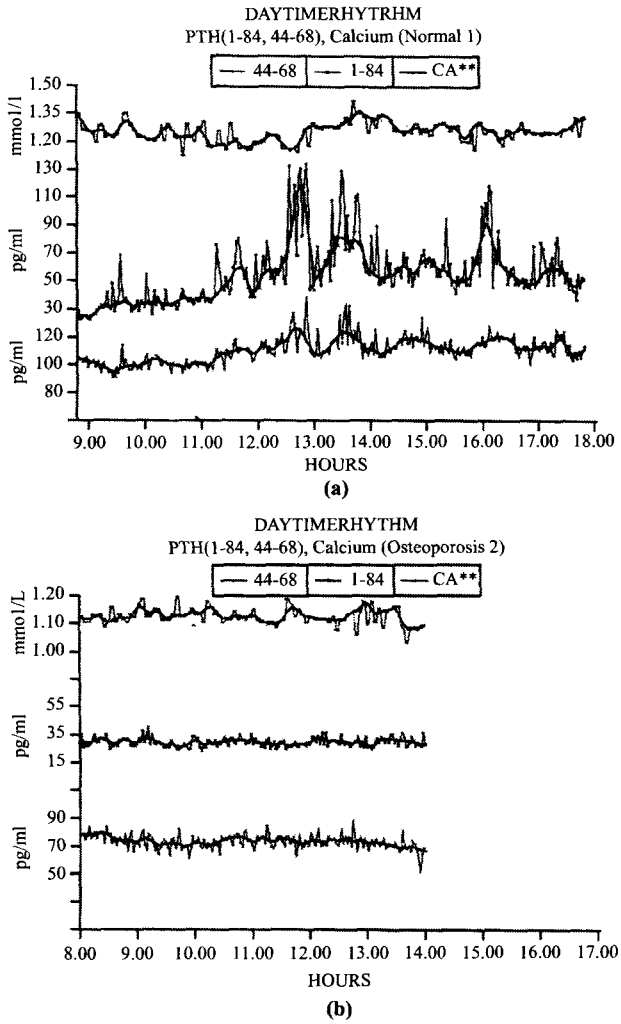

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Figure 1.
Concentration of calcium, parathormone and its metabolite in health and in severe osteoporosis

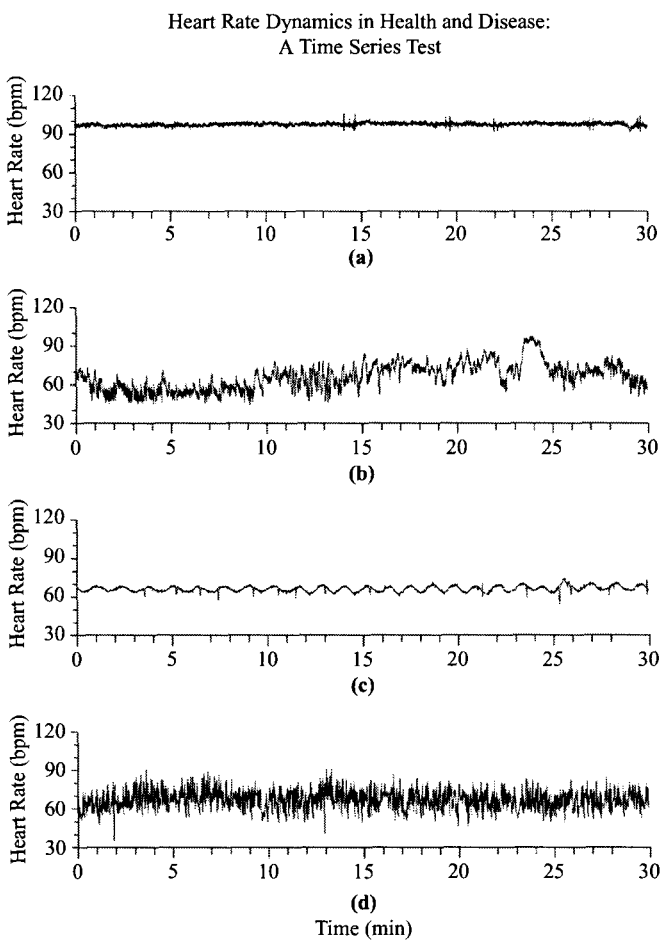

Figure 2.
Heart rate dynamics in health and diseases: a time series test

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arrhythmia, atrial fibrillation, which produces an erratic heart rate. The healthy record, B, far from a homeostatic constant state, is notable for its visually apparent nonstationarity and "patchiness". The healthy pattern is neither rigid nor random (Goldberger *et al.*, 2002).

The Figure 3 shows the behaviour of healthy families. Although more a guess than a measurement, it implies that a "balanced" family is mainly in a sort of "disequilibrium alternating with periods of homeostasis and the fluctuation remains within a manageable range" (Minuchin and Fishman, 1981, p. 22). This contradicts the myth that functioning marriages are free of problems. In contrary, family therapists regard always balanced and harmonious families as potentially rigid. They are endangered to become symptomatic during major transition periods and stressful live events, such as the birth of a child, a member leaving the family, a parent loosing his job, etc.

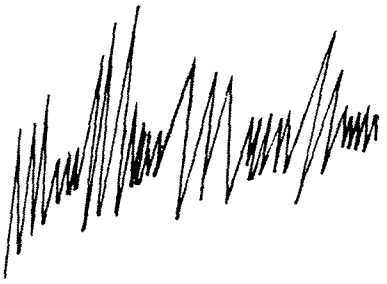

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Figure 3.
Healthy family relationship

This description of rigidity vs robustness seems to fit quite well to the findings in infectious diseases where we probably also see an oscillation between a type 1 and a type 2 reaction and where continuous perturbations with a certain amount of germs seems to be beneficial as long as the immune system is able to keep the effects in a certain manageable range. The lack of such a confrontation might be the first step towards chronic diseases.

Conclusion

The classical concept of physiological control assumes that healthy systems are self regulated to reduce variability and maintain physiological constancy. But the opposite seems to be true (Goldberger *et al.*, 2002). Inducing constancy – often the aim of current medicine – might even reduce robustness. Such a reduction cannot be detected under normal conditions. Normal conditions do not inform us about the fitness of a biological system. Only in challenging situations it is possible to distinguish between adaptability and rigidity. As efficacy control in medicine is mainly done under stable conditions, trials are mostly not able to tell us whether a therapy increases rigidity or adaptation. Even worse, the current concept of efficacy control seems to propagate a learning 0 situation in which an organism reacts the same every day. As learning 0 is mainly found in overstimulated organisms there is some probability that current therapies in order to be regarded as efficacious provoke the rigidity which is then seen as favourable. If this assumption is true, current medicine would partly contribute to a decrease of robustness. This could turn out to be disastrous in times of crisis like war, famine or even under climate change. In order to avoid such possible consequences we propose in every kind of therapy to take the improvement of robustness into account.

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