PFIZER ENDS ALZHEIMER-RESEARCH: AN EMERGENCY SIGNAL FOR MEDICINE AND POLITICS

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Компания Пфайзер закрывает финансирование исследования болезни Альцгеймера: тревожный сигнал для медицины и политики

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Pfizer, the worlds greatest pharmaceutical company (business volume 2016 52,8 billion US$) has ended its efforts in Alzheimer — research. The decision was conclusive: There is no realistic assumption that the invested money can be recovered. The decision was driven by science, not by costs or a lack of qualified scientists: The currently used scientific views from our world (paradigms) are not adequate for the needed scientific challenge. The relevance of Alzheimer for the world wide level of health — and therefore for the cost of related drugs — will increase dramatically because of the shift in the age distribution. So the level of health will decrease. Both facts should be warning signals for decision makers for the future of medicine and politics to reassess the actually used strategies. There is hope if one were able to undertake the following two steps: first to develop a more appropriate paradigmatic model and second to transfer it into specific applicable tools. The «Extended View» is such a paradigmatic model. The model is a matter of further development within IAS-HE and Sechenov University. It is matter of interdisciplinary discussions e.g. within the Russian Academy of Science. Principles of the model are presented.

Keywords: Pfizer, Alzheimer-research, theory of science, natural- and non-natural sciences, theory of principles, paradigm shift, evolution, epiphenomenon, paraphenomenon, Extended View, health promotion, wellbeing.

Pfizer, крупнейшая фармацевтическая компания мира (объем бизнеса в 2016 г. — 52,8 млрд. долларов США), прекратила свои инвестиции в исследования болезни Альцгеймера. Решение было окончательным: нет реалистичного прогноза того, что вложенные средства могут быть когда-либо возвращены. Решение было обусловлено научными выводами, а не затратами или нехваткой квалифицированных ученых. Используемые в настоящее время научные взгляды из нашего мира (парадигмы) не подходят для необходимого научного вызова. Медико-социальная значимость болезни Альцгеймера для здоровья населения в мире и, следовательно, стоимость связанных с ним лекарств резко возрастет из-за изменения в распределении возраста. Таким образом, уровень здоровья будет уменьшаться. Оба факта должны быть основанием для лиц, принимающих решения, о будущем медицины и политики, чтобы переоценить фактически используемые стратегии. Однако есть надежда на иное развитие событий, если предпринять следующие два шага: сначала разработать более подходящую парадигму, и во-вторых, перенести ее в конкретные применимые инструменты для охраны здоровья и лечения человека. Теория «Расширенного взгляда на человека как эко-био-психо-социальную сущность» — такая парадигматическая модель. Модель является предметом дальнейшего развития в трудах ученых Международной академии наук и Сеченовскго Университета. Это вопрос междисциплинарных обсуждений, например, в рамках семинаров и конференций Российской академии наук. В работе представлены и обсуждаются основные принципы модели «Расширенного взгляда».

Ключевые слова: Пфайзер, болезнь Альцгеймера, теория науки, естественные и гуманитарные науки, теория принципов, сдвиг парадигмы, эволюция, эпифеномен, парафеномен, расширенный взгляд, укрепление здоровья, благополучие.

1. The issue:

Pfizer, the world greatest pharmaceutical company (business volume 2016 52,8 billion US$) has ended its efforts in Alzheimer-research. Austria has 8,47 million inhabitants. 100.000 of them are in Alzheimer therapy. The costs for their care has been about 1,2 billion US$ for the year 2016. 2050 230.000 Austrians will be in therapy — because of the shift in age distribution [1]. Similar processes are to be expecting all over the modern world. The market for drugs for Alzheimer is actually gigantic and will increase astronomically: But the argumentation of the president of Pfizer Worldwide research and Development is conclusive: The decision was driven by science, not by cost. The fundamental scientific tools available will not lead down a path cost effective enough

to ever recoup the company's investment [2]. This demonstrates the following: It is not a lack of money, nor a lack of highly qualified scientists. It's not a lack on technical equipment. The utility of currently used tools based on theories on science (epistemology) and paradigms are obviously insufficient for Alzheimer[1].

It is obvious: As a result, the level of health will decrease in many countries. The level of health is internationally accepted as a measure for the efficiency of politics in general. [WHO H21]. Therefore, politicians are also responsible to fight with adequate strategies to inhibit this disaster. More money for the current type of research would not be the adequate answer.

2. The Answer: «Theory of Principle» and Transfer Into Tools for Applied Science

Hence, we need adequate theories — maybe thanks to the use of «theories of principles». This technique was developed by Einstein and enabled him to create the Relativity Theories [3]. His principles (see point 5.1.) should enable us to create a joint scientific approach for all medicine and health related disciplines.

2.1. Prerequisites for a comprehensive paradigmatic frame

The prerequisites for such a model would be:

- Not to lose at any time power to serve patient and clients. Therefore, the proposal must be compatible with the currently used sectoral paradigms and
- The model must be able to bridge the currently given gaps e.g. between natural and non-natural sciences.

3. Analysis of the Power of the Actually Used «Theories» Thanks to a Metaphor

3.1. The metaphor of a perforated barrel

Assume the power of sciences in a comparison of a barrel which enables us to inhibit the seepage of lifesaving water. The bottom and the next part of the staves are totally tight. But as higher the staves are as more perforated are they. The highest barrel hoop is linked with the whole barrel just with few staves. As higher the level of water is rising as more water will flow out and will seep away. Nearly the whole additional water will flow away if the water level has come to this area with only few staves.

Now we attribute health problems to the height of the barrel: Health problems based just on classic physical reasons are on the bottom: We can calculate in every single case if a bone will break or not because of fall, if we have just the physical characteristics. Our predictions will be a little less exactly for classic chemical interactions, e.g. of a trop of acid on the skin. The predictions will be much more unsecure in cases of the interaction of chemicals — e.g. a poison — within bodies. Then we have to consider the biological variabilities. We cannot predict which rat will die in a study for dosis letalis 50. But we know the reason of death: The effect of the poison.

Health problems are settled in the barrel another level up if they deal with interactions with subjective valuation and behavior. The level of explanatory power must be changed in principle: We have to use epidemiological studies and shift from causality to risk. Remember the results of studies about differences risks for Coronary Heart Diseases (CHD) in different classes of clerks: The risk factors could be confirmed and enable us to use them for problem-oriented health concepts. But the risk factors could only reasonably explain about 50% of the observed CHD.

The explanatory power of the current available scientific tools is falling dramatically if the health problem deals with the highest level of the barrel. Here just few staves block the pouring out of water. We have to attribute the research of Alzheimer and of the related drugs to this level. The research is based on Cluster methods. That means that just significant statistic correlations between measured variables can be used without any assumption about a causal connection between them. Therefore epidemiological studies are indispensable to give the background for such correlations, too, but just to invent clusters: So «insufficient» studies are also now useful. The process from such information up to the development of substances, which fulfill the criteria to be accepted as a medical drug is extremely unsecure. Therefore Pfizer came to the conclusion that a correct cost-benefit calculation is not possible.

So, a new reason for the need of a better paradigm (according to Th. Kuhn [4]) is obvious: There is an urgent problem for the level of health in the society. But the current paradigm gives no realistic hope to cope with it even you use all available resources.

But the classic paradigm shift seems to be not adequate: The neglect the old paradigm and substitute all with the new one. The explanatory power of the old and currently used paradigm is sufficient for many health problems. Remember the unbelievable progresses thanks to the current one, e.g. for imaging methods, in surgery etc.

3.2. Analysis of the metaphor

3.2.1. The restrictions of the explanatory power thanks to the used energetic-materialistic monism

Monism is based on the assumption that all can be explained with just one substance. All abilities to be effective and therefore all qualities and quantities are based on this substance. Energetical-materialistic monism is based on the position that energy and its expression as matter is sufficient to explain all in our world. Recent natural science is based on such a materialistic substance monism.

Nowadays no natural scientist will deny that information related processes are part of our world, e.g. his personal creative thinking. Such processes seem to be not suf-

[1] Einstein summarized these epistemic and ontic aspects within his understanding of «theory» and pointed out: «The theory defines what you can observe». The term «theory» is used in this paper according to Einstein.

ficient to be explained just thanks to matter or energy. Natural scientists handle this dilemma with two techniques.

a. Not energetical or not material aspects are postulated as prior postulate:
Any scientific discipline can choose the starting position without a need to explain where the assumed characteristics are coming from. Just one example:
Immunologists postulate that Antigen AG and Antibody AB can observe each another, are able to move and to guide their movement to each other and to interact. And they accept that the meaning of an identical structure e.g. of a poll of birch, can be modified even for the identical Individual. They call this «sensitization» and «de-sensitization». They describe which applications of energetical-material components — sometimes associated with subjective aspects — are linked with these processes. This is helpful in therapy and prevention. But it is not matter of immunological research to discussion «for what» these terms are staying and thanks to what kind of ability AG and AB can cause these phenomena.

b. Within the application of the sectoral science: Epiphenomenon
The term «epiphenomenon» allows to summarize with one word processes in which the immaterial aspect of a phenomenon can be neglected: The shadow is the classic example for an epiphenomenon: Every solid matter and therefore every dog cause an observable shadow if it is exposed to light: The dog can move its solid structure: Therefore the shadow is also moving — without any activity of the shadow. It is obvious: It is sufficient to attribute just to the dog the ability for movement. The change in the position of the shadow looks like «as it would have the ability to move itself». This model is applied as part of the paradigm to any not energetical process. Therefore the paradigm allows to exclude the question about the nature of any immaterial process. The predictability of the observable result is accepted as sufficient cause to explain these processes just with the material nature of the actors (e.g. the poll of the birch and the person). But that is adequate to deal with interactions between from the evolutionary point of view very old actors like light and matter. This ongoing can cause inacceptable reductionisms of other interactions.

c. Paraphenomena: Material aspects can be negligible and «stay just for meaning»
The term «paraphenomenon» is proposed to summarize processes with one word, in which the material aspect of a phenomenon can be neglected. Such situations are quite common in the daily life of a medical doctor. I want to explain it with two bank notes. Both have the same size and consist of the same material. But there two different values printed on it: For example 100 and 10. The value is identical and negligible of the two pieces of paper. But you can pay ten times more with 100 thanks to the social consent. Social consents are prerequisites for paraphenomena between persons or social structures.

3.2.2. Linkage to evolutionary processes

• It is obvious: Epiphenomena occur in relationship of evolutionary ancient interactions, e.g. between light and structure. Paraphenomena are to be expected just in the relationality of entities on a very young evolutionary level.

• The predictability of processes is also depending on the evolutionary nature of the related actors: The bone fracture is based on the interaction of two ancient aspects: The gravitation and the «solid body» bone. The result can be predicted in every single case if the physical parameters are known. Totally different the situation e.g. with Alzheimer. The processes are linked with — from the evolutionary point of view — youngest abilities. This shows the connection between causality and predictability on one hand and evolution on the other hand. Starting point is strong causality within — from the evolutionary point of view — ancient interactions. Actual endpoint is senselessness just to create assumptions about causal connections for scientific studies. This is affected by processes which are interlinked with the — from the evolutionary point — youngest efforts. So we are forced to use cluster methods.

4. Conclusions

Therefore the challenge is to create an adequate paradigmatic frame. Models would be only adequate if they

a) exclude even a temporary decrease of the actually available power to serve patients and clients
b) and would be able to link on a causal level the up to now incompatible but indispensable health related sectoral scientific disciplines.

Ad a) Therefore the intended paradigmatic position has to be compatible with the paradigmatic positions of the different health related sectoral disciplines. Einstein has developed a tool to link the former incompatible theories of mechanics and electromagnetism thanks to the use of a theory of principle. We have adapted this tool according to the special demands of medicine and Public Health.

Ad b) All health related theories are based on the assumption to deal sufficient with the consequences of the evolutionary process for the specific field of medicine. This collective position offers the option for a joint fundament for all disciplines. We have to invent a model which is not only able to make plausible the autopoiesis of different species, but also the self-creation of life from not living ances-

tors. The model has to make conclusive also the further evolution to culture and virtuality.

c) It is indispensable that the model can make plausible, why something will takes place and can therefore predicted, other aspects can be assumed on the basis of risk, and others are uncertain in principle[2].

5. Proposal for a Solution: Extended View

5.1. Interlinkage of both prerequisites

Both prerequisites — the joint evolutionary nature, the linkage of former incompatible theories — can be handled thanks to an extended understanding of the proposal of Einstein how to link former incompatible theories thanks to the technique of «theory of principle». But a short introduction into it before:

a) Einstein started his argumentation with the knowledge that any word is a «free invention of the human mind». Therefore any scientific term, numbers, symbols etc. and therefrom derivated natural laws, theories including paradigms are also «free inventions». Their justification is the increase of power to deal with daily life — or with scientific problems. Therefore only inventions are to accept which can be enforced e.g. thanks to empirical data.

b) Terms focus on selected aspects and skip others of more complex processes. Therefore e.g. the terms, formulas etc. of Newton focus on «mechanical» aspects of «physical movement» and the formulas of Maxwell on «electromagnetic ones». Therefore the incompatibility of Newton's and Maxwell's formulas is not a surprise. But the much more complex nature of physical processes is not in contradiction. We have to expect similar focus and inhibition e.g. in natural scientific based medicine and psychosomatic and social medicine.

c) Einstein used these two positions for a technique to transfer established but incompatible theories into a «theory of principles»: He proposed to invent more fundamental terms and formulas «behind» the formulas of «Newton» and «Maxwell» which could substitute as well the formulas of Newton and as of Maxwell. This is the Special Relativity Theory (SRT): The physical processes are expressed so general that the characteristics of solid bodies (of mechanics) and of electromagnetic waves are skipped out of the formula of the SRT.

We can interpret this line of argumentation as the description of an evolutionary process. Then we substitute Einstein's «behind» with «evolutionary older». Then the SRT describes the physical processes of the precursor as well of electromagnetic waves as of solid bodies. This is in a good agreement with the standard model of cosmology. The same principles of «energetic fields» have to be to expect as well for electromagnetic waves as for solid bodies. «Maxwell» covers only the characteristics of the evolutionary younger electromagnetic fields and «Newton» only the specific characteristics of the evolutionary younger solid bodies. Similar specifications are to expect in consequence of all further emergent processes from the solid bodies up to the autopoiesis of human persons.

Therefore it makes sense to use «evolution» as starting point for a Theory of principle.

5.2. An Extended View of Evolution:

We could make plausible that Einstein's «behind» can be understood as a description of the follow up of an evolutionary process. This gives the hope that his assumptions can be used for a Theory of principles which is based on evolution up to the occurrence of persons. But we have only a description actually. A description is not an explanation. We should not expect an understanding of the causal linkage between the actual not linked sectoral disciplines of medicine without a proposal to explain the nature of the evolutionary process. Now we have such a model just for the understanding of evolution of living beings, but not for the periods e.g. without genes. We need a more general view of evolution. This should make plausible also why aspects can be predicted, others can be handled with risk and others are in principle uncertain. This view should be powerful enough to explain the self-creation of fundamental novelty like the creation of life from not living precursors. It is not a fundamental novelty, if the modification enables just a better use of former given or help to survive.

Such a model is possible. I will demonstrate this on the example of chess.

Recognize the game chess: There are endless options for figures and playing fields which can be made from wood or stone. There is no logic reason to deduce just 8 to 8 fields in black and white or why a «horse» can only move two forward and one to the side or one forward and two to the side. But the subunit constituting consents between persons, to accept these agreements and neglect all other theoretically possible options, creates on one hand the subunit «chess-players»[3]. It makes predictable on the other hand that any chess-player, who touch a «horse» has to move his «horse» exactly according to the subunit constituting consents. But nobody can know which correct option of movement a chess player will use. The expert can make prediction just on the basis of «risk» thanks to observations and experiences. But sometimes

[2] «It would be a poor joke, if a part of our world would be put in order in advance and another part not; if a part of that which happens has to happen, but another part has not to happen». Voltaire. — «But strange to say: we live today in this fanny world, which Voltaire describes». I. Prigogine, Nobel Laureate und late president of IAS.

[3] This fits to the statement of Einstein, that there is no logic way from the phenomena to the theory. Therefore theories have to be invented. But the invention can be and has to be tested on the phenomena [5].

the father is using a «stupid» option. Maybe he is too tired. Or the father is willing to let the son win with the — evolutionary higher — intention, to motivate the son to «love» to play chess and win for his life a source for pleasure and creativity.

Chess demonstrates: The emergent win is from a quality which is in principle different from the qualities of wood or stones. The emergent win cannot be characterized just with matter or energy of the used matter. The prerequisite for the win are agreements about restrictions of options and of the focus just on special options. The evolutionary progress is possible just as a WINWIN constellation: No win without teammate!

Chess has outlasted the inventors of the game because of the willingness to share the knowledge with foreign persons. This is a clever way to have many different partners to play this game. WINWIN is an additional option to the proposals of Darwin and Wallace to explain the autopoiesis of different types of species. And WINWIN allows making also plausible the self-creation of not living entities and their relevance as precursors for living beings.

5.3. Extension of principles

The comparison of the invention of chess has restriction for the understanding of an autopoietic evolutionary process. The invention and realization of chess premise the creativity of the originator and of a skilled carver. Such a prerequisite is sufficient maybe to understand evolution in general if you accept intelligent design. It is insufficient to understand an autopoietic process without influence from outside. Such a model would be conclusive if you accept that the given entities have been able to initiate and realize the novel steps in any period before an emergent progress.

5.4. From these requirements to the invented fundamentals

Now we have carved out the requirement which have to be fulfilled for the basic step of a theory of principles: To invent the principle assumptions which allow declining the processes and entities according to the state of knowledge. Behind that point there are no more inventions allowed according to Einstein: Just logic conclusions and predictions. The — from the point of the first occurrence in evolution — most ancient health related influences are caused by gravitation (e.g. fracture of bone) and light (e.g. to produce Vitamin D). The most recent are influences of virtual reality e.g. of virtual economy. Therefore our model must allow deducing just one evolutionary process «from Big Bang to Big Mac» and further up to virtuality.

This is possible with the following assumptions.

A. We do not accept only the principle of conservation (according to the «classic-physical principle») but also the principle of enforcement/inhibition (according to the «physiological principal» discovered by Pavlov and Sechenov)
   a. Both principles are interlinked: Every focus on one option causes necessarily the neglection/inhibition of its application to other given options because of the principle of conservation.
   b. Therefore we do not live in an ideal world.
   c. A successful adaptation requires the guidance of resource to this option which seems to lead to the intended result.
   d. The evolutionary progress can be understood as a special version of such applications.

B. We accept the position of Einstein (and of many scientists of linguistic) that every scientific term, number, symbol, natural law, every theory, but also every paradigmatic position is a «free invention of human mind». They have to focus on special aspects and to neglect other ones (according to A. a).
   a. The justification for their inventions is to help us to deal better with our problems.
   b. It is not relevant for a medical doctor or any other health care worker to testify «what keeps the world innermost together». Therefor it is not only irrelevant that paradigms are not able to inform us about that. Paradigms can be and should be used — according to the physiological principle — just as tools, to handle as comfortable as possible given problems: It is sufficient to use a water scale and to apply the paradigm «as the world would be a plate», if your problem is to control the correctness of the construction of a wall. This paradigm would not be sufficient if your problem is to find out the shortest way for a flight from Moscow to New York.
   c. Comprehensive simplicity: The available terms must allow to formulate distinct all, what can be observed or logically deduced as different. It is a MUST to introduce a term and to characterize it for proving (especially empirical proving), if this is not possible.

C. Remember Wilhelm Tell: He had the problem to shoot an apple from the head of his son with a crossbow. The problem was not his physical energy but the ability to guide this power goal-oriented.
   a. Therefore there is a need to introduce a term according to B. c. to deal adequate with this additional ability. Therefore we attribute to Wilhelm Tell the (Aristotelian) potentia to be able to cause effects.
   b. Potentia is all the time full in action.
   c. We distinct two fundamental types of effects: energetical ones (thanks to «energy») and meaning related ones (thanks to the now postulated «discrimination ability»). «Ability» is not «substance»! Therefore this is a substance-monistic position and therefore without a linkage to Vis Vitalis.
   d. Discrimination ability was sufficient characterized and successful empirical and logic proved. The additional power allowed to explain e.g. the deviation of observed and predicted mortality rates in survivors of Hiroshima and Nagasaki. The additional power resulted in the assumption that ill-

nesses can be caused not only because of a lack on energetical-material resources but also because of a lack of discrimination ability. This effect is causal independent of the reason for the lack. (causal unspecific health effects) [6a—c]

6. The General Paradigmatic Frame and Its Transfer Into Health Related Application

6.1. From Big Bang to Big Mac and Virtual Economy for a better understanding of health, illness and recreation in five steps thanks «tools for thinking»

I am very sorry that I had to present to you so many aspects which seem so far away from medicine. But you should know: I had to start with these types of fundamentals because of the fact that the restriction of the recent medical science is based on the recent used philosophical self-understanding of science: The substance materialism and its consequences. Pfizer teaches us: there is no realistic hope to deal successfully with e.g. Alzheimer. The presented paper is just a short introduction into the fundamentals of the whole health related model. But remember Gustav Liebig: Nothing is as practical as a good theory.

The way from the fundamentals to the applied aspects is long. The «Extended View» covers therefore five steps.

a) The fundamentals of the Extended View (FEV):
This parts deals with epistemological, ontological and logic tools and their ethical aspects
b) The General Extended View (GEV),
This focus on the evolutionary process of the self-creation of entities from «Big Bang to Big Mac» and further on up to virtual worlds including virtual economy
c) The Special Extended View (SEV)
This part focus on the meaning oriented evolutionary process to make plausible the person as a social being and its interactions with and expectations on her/his different environments
d) The Applied Extended View (AEV)
This focus on the «physiological» [according to the Russian understanding of physiology] consequences of a — c for an extended understanding of health, illness, promotive and preventive effects
e) Transfer to specific applications actually: CES (Comprehensive Extended Social Medicine) and EVPH (Extended View of Public Health)

6.2. Examples for the scientific discussion.

The topics a—d are matter of the research work and of a special teaching offer of the Institute of Normal Physiology of Sechenov University. They are integrated within the discussions in the Russian Academy of Science. Introduction papers are published e.g. by the Russian Academy of Medical Science and Russian Academy of Sciences in the Sechenov Lecture 2004 [7]. Different publications are also available in the Herald of the Russian Section of International Academy of Science — Health & Ecology and other peer reviewed journals.

So there are papers e.g. about the epistemic and paradigmatic aspects [8, 9, 10], about the power of the Extended View as tool to improve interdisciplinarity between different sections within the Russian Academy of Science [11], as tool for land use planning with regards to health and culture for UNESCO [12], about the compatibility of «discrimination ability» and «information» [13], to point out the linkage to placebo and toxicopy [14] with its consequences for the medical expert in the legal procedures [15], about health promotion [16], social scientific aspects [17], about physiological aspects [18, 19] etc.

7. The Frame of Power

The listed papers dealing with the transfer to specific applications (step e) are related primarily to social medicine and Public Health. This shows the general and actual given borders of the model: The Extended View is primarily a paradigmatic frame. The general transfer into applied aspects is to expect therefore just on the basis of fundamental subsystem constituting consents and the empirically proved prerequisites, e.g. the assumption that the capacity of the available discrimination ability is restricted. The different indispensable and powerful sectoral disciplines in medicine are using much more specified paradigms as those which are needed for the General and Special Extended View. These sectoral specialist paradigms allow on one hand to skip out aspects. On the other hand there are experiences of the outputs of the related evolutionary progresses. Just the experts of these sectoral disciplines have the experience of out-coming phenomena. Therefor these experts are able to extend their scientific options with the general positions of the Extended View. This should not be expected by experts of physiology, social medicine or public health. Therefore we are not able to answer where Alzheimer is coming from and how to deal with it specifically. But we could use the Extended View for predictions about causal unspecific effects and prove it in a clinical study in patients with dementia: Their efficiency for memory could be increase thanks to an increase of availability of oxygen after training with technology, which offered hyper-, normo- und hypoxic conditions [20].

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