From:

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Implanted Minds

The Neuroethics of Intracerebral Stem Cell Transplantation and Deep Brain Stimulation

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Intracerebral interventions raise particular ethical issues. For instance, attempts at replacing lost or altered brain cells with the help of stem cells or the therapeutic application of Deep Brain Stimulation would have morally relevant implications. Many medically relevant questions and ethical concerns need to be clarified before these intracerebral interventions can become routine procedure: If the brain is conceived as the carrier of an individual's personality or of the self then operations on the brain can be seen as intrusions upon one's personality. The book addresses historical, philosophical, social and legal implications of these new developments in the neurosciences and aims at resolving some of the dilemmas that go hand in hand with »implanted minds«.

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Introduction

HEINER FANGERAU & THORSTEN TRAPP

Regenerative Medicine, Deep Brain Stimulation (DBS) and Neuroethics are three expanding areas of study. Regenerative Medicine and DBS are novel biomedical technologies with therapeutic potential, while Neuroethics is a collective term used to describe the social and philosophical implications of manipulating the brain and mind. These three topics are closely inter-connected. For example, Regenerative Medicine or DBS can be applied to the Central Nervous System (CNS) to control or treat abnormal brain function or a distressed mind. This situation raises special ethical issues concerning the possible influence of electrodes that act upon neural networks or stem cells that become integrated into these networks and their possible influence on the patient's personality. For example, does the integration of stem cells or electrodes into the brain change the concept of a neural system? Does a neural system containing foreign cells or electronic devices differ from one that does not contain them? These are the questions the book addresses from a practical, theoretical and ethical viewpoint. Furthermore, a historical perspective of the social accountability and hopes and fears inspired by these technologies will also be provided.

Neuroethics was only recently established as a sub-discipline of bioethics. Since 2005, the topic has assumed increasingly more space in bioethical and clinical journals. The American Journal of Bioethics (AJoB), for example, has launched a quarterly supplement called JoB-Neuroethics, and the Journal of Cognitive Neurosciences announced and published a series of essays on neuroethics.[1] Broadly conceived, Neuroethics seeks to examine the philosophical, social and legal implications of new developments in the neurosciences. Whereas some of the topics addressed by Neuroethics may be similar to classical bioethical issues (e.g., informed consent, protection of probands during research, etc.), others lie exclusively within the realm of Neuroethics, most likely because of the special role of the brain in the self-image of man. Arguments in favour of a neuro-exceptionalism closely resemble the discussions surrounding genetic exceptionalism.[2] Both practical and metaphysical problems arising from the neurosciences are discussed well beyond the classic body-mind problem. Examples include legal regulation of psychostimulants, the relationship between the "self" and the brain, free will and the complex connections between behaviour and the CNS. Nevertheless, the need for an autonomous discipline of neuroethics is dubious because the questions it confronts can be answered using classical ethics and the established principles of medical ethics.[3]

Neuroethical topics might be roughly divided into the realms of the social, the political and the "individual self", which encompass clinical practice as well as theoretical issues. On the social and political levels, current neuroscientific research evokes three main topics of discussion noted by the public: 1) functional digital imaging, such as that used in lie detectors or detection of emotions, 2) cognitive performance enhancement, and 3) direct marketing of psychostimulants, which may verge on consumer manipulation. On the level of the "individual self", classic questions concerning free will or responsibility for one's own actions are combined with a resurgence of the debate of the biological basis of these intangible phenomena. Particular points of discussion include the brain's status as the organ of self-representation and its significance for an individual's personality. This special status is challenged by many of the clinical-practical and ethical implications of neuroscientific research and therapy, including predictive testing, which specifically deals with incidental findings or therapeutic measures that influence the self and personality.[4]

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1 C.f. Farah, M. (2007) "Social, Legal, and Ethical Implications of Cognitive Neuroscience: 'Neuroethics' for Short", in: Journal of Cognitive Neuroscience 19: 363-364.

2 Farah, M.: Neuroethics (2004) "A Guide for the Perplexed", in: Cerebrum 6: 29-38.

3 Birnbacher, D. (2009) "Neuroethics and Stem Cell Transplantation", in: Medicine Studies 1 (1): 67-76.

4 Illes, J., S. Bird (2006) "Neuroethics: a modern context for ethics in neuroscience", in: Trends in Neuroscience 29: 511-517. For an overview

In the near future, Regenerative Medicine therapies will surely come to the fore. In both Neurology and Psychiatry, Regenerative Medicine aims to replace lost or dysfunctional brain cells with transplantation of brain tissue, specifically stem cells, which raises philosophical questions. If the brain is conceived as a component of or as the carrier of an individual's personality or self, then operations on the brain can be seen as intrusions upon one's character. The danger of possible character changes after brain surgery was incorporated as a central theme of neuroethics several years ago.[5] However, the emergence of Regenerative Medicine and stem cell transplantation should revitalize this topic.

A loss of neural cells and/or their normal function underlies many neurological diseases, including multiple sclerosis, amyotrophic lateral sclerosis, Parkinson's disease and stroke. However, there is great variability across diseases in the cause and nature of cell loss. Parkinson's disease entails a loss of dopamine-producing neurons in the striatum by neurodegeneration, whereas cerebral ischemia involves the loss of complete brain areas caused by interruption of their oxygen and nutrient supply. Encouraged by the first clinical successes of Regenerative Medicine, researchers are now seeking to use this technology to target diseases currently lacking adequate treatments, specifically by using naïve or neutrally-differentiated stem cells to replace the lost or damaged cells. Numerous studies have shown that intracerebral transplantation of naïve or neuronally-differentiated adult or embryonic stem cells leads to recovery of function in animal models of Parkinson's disease and stroke. However, the mechanisms that effect functional improvements have not yet been clarified. Intracerebrally-implanted stem cells may take over functions lost due to disease, perhaps by integrating into existing neural networks. Moreover, transplantation most likely enhances endogenous regeneration by activation of growth factors. Patients suffering from Parkinson's disease or stroke already receive cell transplantation therapy in clinical studies, though how these treatments mediate improvement still remains to be fully established. In addition, these therapies evoke many ethical questions. If foreign neurons, which possess their own genetic programming, are integrated into neural networks that constitute intrinsic factors of a person's character, and this intervention changes neural circuit function, does this

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of different issues and a comprehensive bibliography see for example Saskia K. Nagel (2010) "Ethics and the neurosciences. Ethical and social consequences of neuroscientific progress" (Paderborn: Mentis).

5 Northoff, G. (1996): "Do brain tissue transplants alter personal identity? Inadequacies of some 'standard' arguments", in: Journal of Medical Ethics 22: 174-180.

entail alteration of the self? Is there a difference between the replacement of degenerated neurons with non-integrating cells that solely secrete neurotrophic factors as a sort of mini-pump and stem cells that integrate into and re-establish or reorganise neuronal networks? In this context, special attention must be devoted to stem cell-derived neurons that have neuroendocrine function, since relatively few neuroendocrine cells can impact signalling of a magnitude of neurons via secretion of neuroactive hormones.

Finally, for more than 60 years, neuroscientists have attempted to control human behaviour, motor and sensory functions using DBS. These attempts have raised public concern in the past, including Robert Heath's early studies, in which electronic brain stimulation was used to cure schizophrenic patients or septal stimulation was reported to induce heterosexual behaviour in a homosexual man.[6] In addition to raising questions of autonomy, informed consent and human dignity, the public has been concerned about controlling the mind by electronic stimulation devices. Jose Delgado went so far as to deduce from his own and other studies on electronic brain stimulation that it might be an ethical imperative to control the mind with the help of DBS in order to create a "psycho-civilized society".[7] However, Delgado himself acknowledges that "the phrase 'control of human behaviour' is emotionally loaded" (p. 247). Even today, the idea of controlling the mind or changing personality underlies many of the fears and ethical issues associated with DBS. As with intracerebral stem cell transplantation, the view of the self and the possibility that brain stimulation may change the self frames the theoretical and ethical discussion in clinical practice.

To conclude, the "implantation of minds" involves control of the brain and mind. Whereas the implantation of stem cells seeks to control loss, degeneration and regeneration of cells, DBS aims to control movements, thoughts, emotions and behaviour. The ethical implications of both approaches to induce technology on the brain and mind are discussed from different perspectives in this book. The first section is mainly dedicated to the implications of intracerebral stem cell trans-

6 Heath, R.G. & H.C. Becker (1954) "Studies in schizophrenia: a multidisciplinary approach to mind-brain relationships" Cambridge, MA: Harvard University Press. Moan, C.E. & R.G. Heath (1972) "Septal stimulation for the initiation of heterosexual activity in a homosexual male", in: Journal of Behavior Therapy and Experimental Psychiatry 3: 23-30.

7 Delgado, José Manuel Rodríguez (1971) "Physical control of the mind: toward a psychocivilized society" New York et al.: Harper & Row (First Edition 1969).

plantation, while the second section discusses DBS. Nevertheless, the two sections are inter-related.

The book begins with an overview by Heiner Fangerau of the beginnings of Regenerative Medicine and the paradox of a technical fix for ethical dilemmata caused by applying Regenerative Medicine to the brain. Next, Josef Quitterer discusses whether intracerebral interventions can change the self. This reasoning is continued by Jan Goldstein in his analysis of Parfit's concept of personal identity and its implications for stem cell transplants. Possible changes in personality are also the topic of Christian Bührle's deliberations about the potential negative impact of stem cell grafts on plasticity. This issue is further discussed by Jens Clausen from a medical-ethical perspective. With his reasoning about creating "part-human beings", he introduces the ideas of speciesism and first-in-human trials, which are discussed in detail by Alexandre Mauron and Samia Hurst in their ethical analysis of innovative cell therapies for Parkinson's disease. Finally, Mirjam Rupp and colleagues ask opinions and expectations of novel therapies of patients suffering from amyotrophic lateral sclerosis, a possible target for Regenerative Medicine.

Mareke Arends and Heiner Fangerau introduce the section concerning DBS with synchronous and diachronous perspectives on the use and ethics of this technology in psychiatry. Next, Frank Stahnisch discusses the ethical and epistemological issues of DBS from a historical perspective. Christian Bührle then raises the question of the possible danger for personality inherent in the application of DBS. This topic is expanded by Sabine Müller in an essay on the effects of DBS on personality and their evaluation according to the principles of biomedical ethics. Thomas Hälbig discusses ethical lessons from DBS in movement disorders, and Jörg Fegert adds an additional clinical viewpoint by examining the use of this technology in children and juveniles suffering from neuropsychiatric disorders with extremely adverse courses. Finally, looking ahead, Dominic Groß calls for the development of parameters that might underlie the social acceptance of neuroenhancement, a possible future application of DBS.

The book is the result of an interdisciplinary workshop on "implanted minds" held at the end of 2008. The overall intention of the publication this book is to give an interdisciplinary overview of the problem of implanted minds from different perspectives, and we hope that these essays will foster further research and discussion on this subject, as intracerebral transplantation of stem cells and DBS will certainly continue into the future.

We owe our gratitude to all the contributors and to Laura Schütte for helping to realize this publication.

For the editors
Heiner Fangerau and Thorsten Trapp

Brain, Mind and Regenerative Medicine: Ethical Uncertainties and the Paradox of their Technical Fix

HEINER FANGERAU

Introduction: The Paradox of a Technical Fix for Some Bioethical Dilemmas

"Regenerative Medicine" is a new branch of medicine that reflects a rekindled interest in healing or replacing lost, pathologically altered or degenerated tissue or organs: their *restitutio at integrum*. Although regeneration and medicine are closely related, they have rarely been directly associated with each other. The relatively new term "Regenerative Medicine" was probably coined by Leland Kaiser around 1992 and was popularised by the American researcher William A. Haseltine in 1998 (Lysaght and Crager 2009).

One of the few early books that directly addressed the central role of "Regeneration and Transplantation in Medicine", was published in 1910 by Dietrich Barfurth. This book summarised the main features of research and practice in Regenerative Medicine, as they had been established at the end of the 19th century and as they are still valid today. Barfurth stated that transplantation always requires surgery and that regeneration usually does, and while especially the joint procedure of the implantation of embryonic tissue is effective, both regeneration and the transplantation of embryonic tissue are closely related to metaplasia and tumorigenesis. Barfurth also raised the ethical issue of researchers conducting regeneration and transplantation experiments. For his perspective research in that area to gain knowledge was solely possible on plants. According to his views research in animals and humans would morally require the higher aim of healing. Not the gain of knowledge but healing as "the intrinsic object of medicine", and benefit for the human being should be the ideal behind the application of such techniques (Barfurth 1910: 5f.).

The modern term "Regenerative Medicine" embodies this means-end-orientation by combining the positive connotations of biological regeneration research (youth, health, restitution) with the medical goals of healing. Haseltine's popularisation of the term occurred in the same year (1998) in which human embryonic stem cell cultures were first established by James A. Thomson (Thomson et al. 1998). This constituted a breakthrough opportunity for the medical use of regeneration research, but at the same time an ethical challenge concerning the use of human embryos for research purposes. The moral uncertainty related to these approaches does not question the goal of regenerative therapy, but rather pertains to the approaches being used to reach this goal. Principally, these concerns can be traced back to two different problems: 1. Beings are created which do not normally exist in nature, namely clones; and 2. the exploitation and disposal of potential human life – that is the embryos that are generated by therapeutical cloning or by stem cells, theoretically could become human beings, if implanted into an uterus (Edwards 2004; Gilbert 2004). Beyond these moral uncertainties, there are also technical uncertainties. For example, stem cells implanted in rat brains can be tumourigenic, an objectionable and unintended effect (Shih et al. 2007). Thus, the question is not just "is biomedicine allowed to do what it can," but also "can biomedicine do what it portends to do?". As a consequence, Barfurth's older dilemma of experimentation with living species versus the aim of healing resurrected directly linked to Regenerative Medicine.

Many subsequent statements by scientists and politicians have defended the necessity of regeneration research for the development of cures for e.g. Morbus Parkinson, Alzheimer's disease, stroke etc. (see for example Andres et al. 2008). Innovations such as the use of adult stem cells, artificial parthenogenesis, and the reprogramming of adult cells have sought to circumvent the ethically critical use of human embryos. These alternatives have been embraced by political figures and the public as welcome solutions to their ethical concerns (Fangerau 2005). Headlines such as "Testicle stem cells avoid 'ethical problem'" (*Washington Times*, October 9, 2008) appeared in many newspapers. However, all of these solutions obscure the issue that regeneration's objectives may lead to the development of germ cells and embryos raised from reprogrammed body cells.

A “means-end-orientation” underlies the two main justification strategies surrounding this issue, which are strikingly similar to those Barfurth used one hundred years ago: the first strategy recalls the goal of all research (which is knowledge in general and healing in medicine specifically), and the second promotes acceptance of biotechnical solutions for bioethical questions. The identification of continuities and discontinuities in the acceptance of these strategies is crucial for a detailed understanding of current ethical challenges like the implementation of stem cell surgery in the brain or deep brain stimulation. It may also provide insight into the development of medicine by examining the simultaneous rationality and paradox that:

a) the goal of developing cures can supersede ethical concerns about research, and b) biotechnical solutions for biotechnically induced ethical problems are accepted without scrutiny of the underlying problematic bioethical beliefs.

This article analyses the historical contingency of the acceptability of the “means-end-orientation” in medicine, focusing on synchronic and diachronic shifts in action perspectives to explain the rational appearance of a moral paradox. It aims at explaining why technologies like Regenerative Medicine or deep brain stimulation meet public fears although their intention is delivering cures. After a brief overview of the history of regeneration research and its connection to brain physiology around 1900, two contradicting views of nature will be analysed in order to contribute to current debates about Deep Brain Stimulation and Regenerative Medicine in connection with brain tissue. Prevalent around 1900, these views of the brain and mind adopted differing perspectives on appropriate medical approaches to diseases of the brain and the circumstances under which research for the sake of medicine is acceptable. These views are used as a foundation to explore the underlying reasons for: a) shifts in the acceptance of electrical stimulation, regeneration research and neural tissue engineering over time; and b) the insufficiency of technical solutions and means-end-orientated justifications in overcoming moral uncertainties about regeneration research and the mind.

Regeneration and World Views

The history of Regenerative Medicine is marked by four trends which needed to come together to give birth to this new branch of medicine: understanding physiological regeneration in living beings, transplantation techniques, cell culture techniques, and fertilisation research. Each of these has received enthusiastic responses and faced ethical scepticism.

Several systematic and comprehensive attempts to characterise regeneration were made in the 18th century. The public responded vividly to the research of Abraham Trembley, René Ferchault de Réaumur, Lazzaro Spallanzani, and Charles Bonnet, viewing their results as miraculous and/or frightening (Dinsmore 1991; Buscaglia and Duboule 2002; Moeschlin-Krieg 1953). The experiments of Trembley and Spallanzani shattered widely held beliefs about the character of living matter and changed some fundamental theories regarding the phenomenon of regeneration. Trembley established the link between regeneration and reproduction, which constitutes regeneration research until today, by artificially producing several new mature individuals by surgically dividing a polyp. On the basis of this link, Spallanzani fostered an epigenetic understanding of development that contradicted prevalent preformistic and predeterministic beliefs about the organisation of life on earth.[1] His discovery that urodeles could regenerate complex forms, such as limbs, contradicted the predominant view that the structures of higher living beings had been preformed in the egg. The doctrine of preformation itself justified the beliefs in predestination, and in the security of animals' positions in natural hierarchies and humans' positions in social hierarchies ("scala naturae", Dinsmore 1996).

Regeneration research coalesced with the evolutionary ideas of the 19th century, and the observation of cell differentiation and proliferation, to question the static world view that had dominated until the end of the 19th century. This caused scientific insecurities and moral uncertainties that repeatedly arose, for example, when Gustav Born reported the creation of chimeras by transplantation of embryonic tissue from one amphibian to another in 1897, when the physiologist Jacques Loeb reported successful artificial parthenogenesis in 1899, when Ross Harrison in 1907 and Alexis Carrel (with Montrose Burrows) in 1911 reported the creation of immortal cell cultures (Das 1990; Fangerau 2005; Freed 2000: 34-36; Landecker 2007; Maienschein 1983; Witkowski 1979, 1983), or when W. Gilman Thomson announced "successful brain

1 For details see Van Speybroeck et al. (2002)

grafting" in dogs and cats in 1890 (Anonymous 1890). The discourse surrounding these scientific events ranged from enthusiasm to scepticism, and the implications for biology and medicine were carefully considered and discussed. While the scientific value of the regeneration experiments was praised, their practical value was doubted even in journals like *Science* (Anonymous 1890). In particular, their ontological implications were widely discussed.

The findings of Jacques Loeb are used here as an example. Around 1900 Loeb announced successful artificial parthenogenesis in sea urchins, and the hybridisation of sea urchin eggs with sea stars. He was also the first scientist to induce embryological development in sea urchins without sperm cells by changing the electrolyte solution surrounding them. He thereby became a celebrated scientist and public figure, appearing on the cover of *Harper's Weekly*. Salacious jokes referred to his work with parthenogenesis because it evoked the idea of Loeb having proved the scientific possibility of immaculate conception. His research on fertilisation and regeneration was compared to the creation of life. The *Boston Herald* published the headline, "Creation of Life. Startling Discovery of Prof. Loeb. Lower Animals Produced by Chemical Means. Process May Apply to Human Species. Immaculate Conception Explained."[2]

Similar to modern scientific discoveries but far more vehemently Loeb's research was popularised not only as a step forward towards medical cures, but also as fundamentally dangerous. The research of other regeneration, transplantation and cell-culture researchers was similarly marked as potentially injurious to human self-image. Soon it was linked to brain physiology and psychology. For example, H. G. Wells' novel *Dr. Moreau* and press reports written about the discoveries of scientists such as Born appealed to basic fears regarding biomedical research. The *Bangor Whig and Courier*, a newspaper serving the predominantly rural population of Maine, linked regeneration research to psychological control over living beings in an article titled, "Monsters to Order. Ingenious Scientists Put Their Wits to Work" (Bangor Daily Whig and Courier, Friday, March 4, 1898: 4). Caricatures depicted scientists' attempts to control regeneration and reproduction, and emphasised their alleged lust for breaking taboos. One satirist sketched Loeb with a cage full of chimeras ("Dr. Loeb exhibits a few of his new creations..."), in which Loeb appears pleased that the chimeras address him as "papa" (Pauly 1987, Fig.11).

2 For a survey, see Pauly (1987); *Harper's Weekly* (13. Dezember 1902: 1936); Boltzmann (1905); *The Boston Herald* (Nov 26, 1899: 17).

Among other journals, the family news magazine *The Cosmopolitan* published by W. R. Hearst in 1912 more clearly expressed the dangers of regeneration research. This journal argued that such research attempted to explain life phenomena with chemistry and physics:

"[…] If you and I are merely physico-chemical compounds, slightly more complex than a potato…what is the basis of our moral code? If man can lump together sand and salt and by pouring water on them create life, what becomes of the soul?"[3]

Such statements reflect the challenges to the contemporary understanding of nature posed by regeneration scientists employing experimental methodologies, such as Born, Carrel, and Loeb. Commentators worried that the new powers of biological research might engender new moral problems, and feared that the new biology would undermine traditional moral values. Especially Loeb fired these anxieties with both his experiments and the promotion of his idea to free the brain from its notion as an ethically exceptional organ differing from other body parts. He argued: "The analysis of instincts from a purely physiological point of view will ultimately furnish the data for a scientific ethics." (Loeb 1900: 197)

The prevalent contemporary "organological world view" did not accommodate these scholars' research questions or their scientific methods of answering them. Briefly, organological world views are characterised by the belief that a vital force binds the individual parts of an organism, and that these individual parts are inextricably intertwined and interconnected. This perspective allows emergent phenomena, ruled by the vital force to join a whole that is more than the sum of its parts. The core disciplines of this world view are theology and philosophy. Its epistemology is marked by holistic tendencies that see correspondences between macro- and microcosm. These create a cyclical relationship between the researcher and the object of research, such that everything in the object is repeated in or has an effect on the researcher. The researcher consequently acts solely as an observer who reports on behaviours in and characteristics of nature.

The bioethical action perspective that is descendent from this world view promotes the respectful preservation of the natural *status quo*. From this perspective, experimental manipulations and attempts to control nature distort the natural world and irresponsibly disarrange its

3 Quoted from Turney (1995). Here, further similar reactions can be found.

wholeness. Goethe articulated this belief in the aphorism, "Nature will reveal nothing under torture; its frank answer to an honest question is 'Yes! Yes! – No! No!' More than this comes of evil." (Miller 1995: 307)[4] This view was often paired with religious orientations that attributed nature's expediency and perfectness to a divine influence.[5]

This pervasive perspective views regeneration research, transplantation, artificial reproduction, and cell culturing not as expressions of creation, but as the destruction of nature and the existing moral order. A means-end-orientation cannot excuse regeneration research within this conceptual framework, even if it offers cures. Technical solutions for ethical concerns are similarly unacceptable. Some researchers were accordingly scared by their own hubris; for example, Wilhelm Roux, the founder of developmental mechanics, wrote the following about his 1888 embryological experiments:

> "[…] I plunged a sharp needle in the frog's egg, not without feeling an inner horror that I dared to interfere in such a way with the mysterious complex of the developmental processes of a living creature." (Roux 1905: 47)

Others debated the organological world view, provoking an ontological clash. Loeb programmatically introduced readers to his early experimentation with organ regeneration in marine animals with the words,

> "I have undertaken the task of finding out whether and by what means it is possible in animals to produce at will in the place of a lost organ a typically different one – different not only in form, but also in function." (Loeb 1891: 1)

For him the aim of his research was not analytical, he had

> "another and higher aim, which is synthetical or constructive, that is, to form new combinations from the elements of living nature, just as the physicist and chemist form new combinations from the elements of non-living nature." (Loeb 1893)

4 For a short analysis of Goethe and his view on nature and "delicate empiricism" as a scientific method see among others the interesting approach by Bywater (2005).

5 A comparison of organological and mechanistic world views and their counterparts has been given by Köchy (1997). A short and precise overview was published by Allen (2005); Müller (2008). The bioethics of organological and mechanistic world views were discussed by Köchy (1998).

Life phenomena were for Loeb physicochemical processes, and he sought to understand their underlying mechanisms by gaining technical control over living organisms. He summarised these ideas in a letter to his mentor, physicist Ernst Mach:

"The idea I have in mind is that man himself can interfere with animated nature as a creator to possibly form it according to his will. This way at least a technology of living things could be obtained. Biologists call it a creation of monstrosities; railways and telegraphs and all the other achievements of the technology of inanimate matter are consequently monstrosities as well, at least they were not created by nature, man did not discover them." (Loeb to Mach, November 11, 1894, DMM, translation by the author)

Loeb further stated that biology would only become a science when abiogenesis was made possible by technical means, and that he wished to apply biotechnology to mental, social, and ethical questions. He argued that human ethics must be the result of chemical processes in the brain, just as human existence was based on physicochemical mechanisms. He believed that humans ate, drank, acted, and reproduced because they were compelled like machines to do so, not for metaphysical reasons (as Loeb named any reason outside of physic-chemical explanations). The same compulsion applied to workmanship, maternal love, a sense of community, and the struggle for justice. Deviations were caused by economic or social conditions, or by genetic mutations (Loeb 1912).

The core disciplines of such a mechanistic world view were mathematics, physics, and chemistry. Its epistemology can be characterised by positivism, materialism, and mechanism, which resulted in a predominantly experimental methodology. The corresponding action perspective used technology to address ethical concerns. Comparison of the organological and mechanistic understandings of nature reveals a fundamental methodological and moral shift. On an ethical level, the mechanistic world view embraced a technical control and authority that had been unacceptable from the organological viewpoint (Table 1).

Table 1: The investigation of nature from a mechanistic and an organological perspective and the following action perspectives

Level of Concern	**Organological Perspective**	**Mechanistic Perspective**
Reference disciplines	Theology Philosophy	Mathematics Physics, Chemistry
Epistemology	Holism Macrocosm / Microcosm	Positivism Mechanism, Materialism
Research method	Observation and description	Experiment und control
Action Perspectives	Respect and keep the status quo	(Bio-)Technology, bioengineering

Intervening in the Brain and Mind

Current developments in stem cell research and related regenerative and therapeutic exploration are predominantly governed by the mechanistic approach. This world view has become the standard and style-forming pattern underlying biomedicine. It has determined the current medical understanding of the brain and has allowed medical interventions such as the implantation of stem cells or electrodes. The means-end orientation is to some extent a legitimate justification for biomedical research, and allows technical solutions to be offered for ethical dilemmas of biotechnological origin without reflecting on technology itself. If technical control can be employed to solve a problem within a given world view, this principle must also apply (however circular) to technically produced ethical problems.

Such principles apply to the exploration of the brain and mind. Loeb argued around 1900 that mind as a function of the brain including memory, psychology, instincts, and behaviour could be explained in purely physicochemical terms. He stated that,

"the physiology of the brain has been rendered unnecessarily difficult through the fact that metaphysicians have at all times concerned themselves with the interpretation of brain functions and have introduced such metaphysical conceptions as soul, consciousness, will, etc. One part of the work of the physiologist must consist in the substitution of real physiological processes for these inadequate conceptions." (Loeb 1900: V)

He thus believed that mind as a brain function is a physical and chemical physiological process, and considered it to be susceptible to the (chemical) instillation of ideas (Loeb 1912: 62), education (Pavlovian conditioning), and electrical or chemical stimuli. For example, Loeb considered the penal code a means to "strengthen the inhibitory associations of weaker members of society" (Loeb 1900: 234; also in more detail Loeb 1899). Almost 70 years later, Jose Delgado proposed that electrical brain stimulation could be used to civilise the human psyche. Adopting a perspective similar to Loeb's, he argued that mind control through the application of electrodes would continue the evolutionary process through mental liberation and self-domination. Such liberation of the brain from biological constraints or innate biological influences could improve society by controlling, for example, aggressive behaviour (Delgado 1969; Horgan 2005). This perspective brings to mind Loeb's statement that, "[…] in the end, science will carry out such a revolution in ethics as it has done in our material life before" (Loeb 1904-1905: 784). Delgado's beliefs were not always taken seriously (e.g. Rothenberg 1970), and the modern understanding of the brain has revealed that it is far too complex to be easily "psychocivilized", as Delgado suggested, nevertheless currently active neuroscientists make statements such as the following, in accordance with Loeb: "If we make statements on freedom of will we apply the conceptual tools from our laboratory to formerly philosophical questions – and for the first time we end up with scientifically based answers."[6]

Conclusion

Many models have been produced to explain the prevalence of materialistic and mechanistic views such as the biomedical research paradigm in Western societies including both aspects the history of ideas and the social history of science.[7] These models agree that developments within the medical sciences cannot be interpreted in isolation, but only within social and historical contexts.[8] Biomedical explanations thus seem to

6 Wolf Singer in an interview, in: *Die Zeit,* 14.07.2005 (Nr. 29) "Wenn wir Aussagen zur Willensfreiheit machen, wenden wir das konzeptuelle Werkzeug aus unseren Labors auf ursprünglich philosophische Fragestellungen an – und kommen dabei erstmals zu naturwissenschaftlich untermauerten Antworten". Translation by the author.

7 For overviews see among others Dijksterhuis (2002); Rothschuh (1978); Wittkau-Horgby (1998).

8 Ludwik Fleck has hinted at this connection very precisely some time before Thomas Kuhn and others (Fleck 1980).

provide an acceptable "rationalization", in Max Weber's sense, as the *primum movens* of Western societies. A rationalising perspective approaches social actions and interactions through calculation (e.g. of efficiency); in this way, it intrinsically contradicts motivations or speculations derived from mysticism, religion, custom, emotion or tradition. Such considerations of efficiency and predictability are central to the modern biomedical approach.[9]

Although the goal of Regenerative Medicine or Deep Brain Stimulation for medical purposes is not questioned, ethical uncertainties about endeavours such as stem cell research or abusing Deep Brain Stimulation for intentionally altering a person's mind persist. Neither the goal of finding cures nor the development of techniques that avoid the use of embryos have overcome basic concerns about the status of nature and human attempts to control nature or human mind. These unresolved issues may indicate the incomplete dominance of the mechanistic model in societal beliefs. The organological, materialistic and mechanistic viewpoints presented here are extreme positions that are often softened or compromised in the reality of the laboratory. For example, Barfurth and Roux articulated such justifications and discomfort when presenting their research. Similarly, current researchers metaphorically invoke the magic of Mother Nature[10] when they have difficulty providing full explanations for the complex processes of life.

Although the mechanistic paradigm dominates the technological sector of biomedicine, its dominance vanishes when medicine is considered in a social context. Critique of the mechanistic model is still a component of normative discussions regarding bioengineering or technical fixes for the human brain. The inherent insecurity in biomedical means – the uncertainty of results of biomedical healing attempts – has also contributed to disenchantment with a purely mechanistic approach. At the beginning of the 21st century, the mechanistic model has lost some of its appeal. The increasingly perceived complexity of life processes, such as regeneration, has impeded simplistic explanations based on causal-analytic calculation. Despite conceptual acceptance of the basic tenets of mechanistic biomedicine, some patients nevertheless feel uncomfortable with an impersonal or analytical treatment option when they are ill. Physicians who have been educated under the bio-

9 For this and the following questions compare the excellent surveys of Hewa (Hewa 1994; Hewa and Hetherington 1995).

10 E.g. "It is certain that many different strategies will be attempted before we can recapitulate even a small fraction of the success and efficiency that has resulted from hundreds of millions of years of research and development by Mother Nature" (Badylak 2005: 36).

medical mechanistic paradigm see the "art of medicine", which is nurtured by organological tenets, endangered by a mechanistically constituted action perspective.[11]

The mechanistic viewpoint thus enjoys broad intellectual and rational acceptance in society, but also contradicts the moral intuition and empirical experience of many people. This disparity is caused by the different speeds at which rationalising processes proceed in biomedical-technical and sociocultural contexts. Following Weber, Jürgen Habermas defined the process of rationalisation as the gradual extension of purposive-rational action into nearly all spheres of social life, even though such action may directly contradict traditional moral values and ethics (Habermas 1969; 1968). Such asynchrony results in areas of conflict. The growth of this area over time due to different speeds of rationalisation processes in the sphere of values and purposive-rational action helps to explain temporal shifts in acceptance of regeneration research and other mechanistic approaches in medicine, as well as the failure of technical solutions and means-end orientated justifications to eliminate moral uncertainties about such research.

Recognition of non-parallel development in the rationality of purposes and values highlights the sociocultural contribution to the growing perception of the limits of the mechanistic approach and the critique of its research goals, such as therapeutic cloning or the fear of mind control due to deep brain stimulation. This process accompanies scientific, biotechnological progress. Uncertainty about the mechanistic world view is growing as its limits become better understood; these limits, in turn, must be considered in relation to the organological perspective. This arena of contradiction may be historically and philosophically examined. Regenerative Medicine and for example deep brain stimulation for psychiatric disorders (which might be understood as mind control) may not continue as a publicly funded field of research unless both purposive-rational actions and traditional concerns can be addressed. The dichotomy between mechanistic and organological world views may thus still need to be challenged, with the goal of their integration. Knowledge of Regenerative Medicine's history and of mechanistic and organological views of the brain and mind may facilitate the future establishment of "implanted minds" as an interdisciplinary field of research that includes neuroscientists, philosophers, and historians of science.

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11 See for example the plea for the integration of holistic concepts and evidence based medicine and the quoted literature in the Journal of Evaluation in Clinical Practice (Miles 2009a, 2009b).

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