Stimulating the Brain
Ethical Perspectives on Deep Brain Stimulation & Nano Scaled Brain Machine Interfaces

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Abstract
This thesis addresses some of the ethical concerns raised by connecting man and machine through so-called Brain-Machine Interfaces, BMIs, elaborate brain implants that may both further our knowledge of the brain and alleviate neurological dysfunction and impairments. The primary foci have been to address urgent and prominent concerns elicited by BMIs; to critically evaluate arguments relevant to an ethical analysis of Deep Brain Stimulation, DBS; and to address and develop ignored or underrepresented perspectives of importance in an ethical analysis of DBS.

The main method used in the analysis is ‘embedded ethics’. This method was developed during the doctoral project, to answer the specific research questions examined in paper I-IV, and builds on methodology such as empirical ethics and casuistry. The purpose of ‘embedded ethics’ is not to derive final conclusions or action guidance regarding a technology as such, but to identify, critically assess and problematize central ethical concerns elicited by new and emerging technologies, and to detect and address the lacunas in the current debate.

Some key contributions of this thesis to the fields of nanoethics, neuroethics and bioethics are: to introduce the distinction between inherent and noninherent ethical concerns to elaborate on upcoming and future ethical concerns elicited by DBS; to identify biases, for instance as regards technology, time, speculative scenarios, and authenticity, that may distort an ethical analysis of DBS; to argue for the duty of ethicists analysing bioethical concerns to acknowledge the necessity of acquiring sufficient knowledge of the scientific/biological subject matter of analysis, knowledge either achievable by being an ‘embedded ethicist’ or through a firm dedication to understanding the particulars and contextual impact factors specific to the subject of analysis.

Key words Brain-Machine Interfaces, BMI, Deep Brain Stimulation, DBS, Neuroethics, Nanoethics, Embedded Ethics, Biases, Authenticity, Inherent Ethical Concerns, Noninherent Ethical Concerns

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ABBREVIATIONS

BCI: Brain Computer Interface
BMI: Brain Machine Interface
DBS: Deep Brain Stimulation
EEG: Electroencephalography
IEC: Inherent Ethical Concern
MDD: Major Depressive Disorder
N-IEC: Noninherent Ethical Concern
NRC: Neuronano Research Center
PD: Parkinson’s Disease
TRD: Treatment Refractory Depression
WHAT IS THE HYPE?

Then the eyes of the blind shall be opened,
and the ears of the deaf shall be unstopped.
Then shall the lame man leap as an hart,
and the tongue of the dumb sing

Isaiah 35: 5-6

Can the blind regain their vision, the deaf begin to hear, a paraplegic person walk, or the silent start communicating? For someone not up to date with the frontiers of science, these scenarios likely sound incredible and for those with a Christian inclination such suggestions may even have a prophetic ring to them. Nonetheless, Isaiah’s vision is now slowly becoming realized by intricate brain implants connecting man and machine, known as Brain Machine Interfaces (BMIs). These BMIs create a direct interface between an electronic device and the central nervous system, allowing them to interact and communicate. Invasive BMIs require a surgical procedure where the device is inserted either into the brain or the spinal cord. Once implanted, the BMI is supposed to remain in the body and is then used for listening to or stimulating the adjacent cells, thus generating the actual brain-machine interaction. There are also non-invasive BMIs, devices that do not require surgery, where the BMI is placed on the scalp.
Some BMIs are acknowledged and well-used in clinical practice, but most applications are still experimental. The first commercialized BMI, the cochlear implant, is an electronic hearing device designed to produce useful hearing sensations for persons with severe to profound neural deafness. Today more than 324,200 people worldwide have received cochlear implants\(^1\), and over 100,000 people\(^2\) use a device, best described as a pacemaker for the brain, known as Deep Brain Stimulation (DBS). At the experimental stage there are BMIs such as retina implants that will provide the blind with rudimentary visual orientation skills, electronic devices designed to improve memory function, and advanced prostheses manoeuvred by neural control, just to mention a few examples. Although it is easy to marvel at the progress already made, research on BMIs is still very much in its cradle, considering some of the expectations of what BMIs can come to make possible.

Does it sound like science fiction? The association would not be surprising considering that BMIs are a recurring theme within the genre. Elaborate fusions of man and machine surface in blockbusters like *The Matrix* and *Robocop*; as do brain implants used for mind control, as for example in the remake of *The Manchurian Candidate*. Conversely, what if we, like the X-Man Jean Grey, could move objects merely by thinking, or, communicate by thought alone? Pure fiction? Though a BMI will not make us telekinetic, the late Matthew Nagel, a paraplegic implanted with a BMI, was in 2004 the first man to use a brain implant to control external devices by thought alone when he manoeuvred both a computer cursor and a hand prosthesis.\(^3\) Another example is the DARPA project ‘Silent Talk’, where an electroencephalography (EEG)-based BMI is hoped to enable soldiers to communicate wordlessly on the battlefield via ‘telepathy’, thoughts picked

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\(^1\) These numbers are from December 2012. (NIH, 2013)

\(^2\) Medtronic, 2013

\(^3\) Hochberg, et al., 2006
up by the EEG and then transmitted to other soldiers. Some BMI proponents even have more far-reaching visions. They suggest that this technology should be used to facilitate an ‘upgrade of man’ and create so-called ‘enhanced humans’, or even Humanity 2.0, beings envisioned as having unprecedented or entirely new senses and experiences. Hence, boosted by staggering possibilities, biblical overtones and colourful fiction, the emerging research on BMIs is an attention grabber where the line between science and science fiction easily gets blurred.

Given these prospects, thorough ethical analysis is called for. However, this analysis cannot be undertaken until facts are separated from fiction and it is made clear what research on BMIs de facto can and cannot make possible. Thus, the first step in an ethical analysis is to put science prior to speculation, and cut a sound path through the scares and hypes that frequent the headlines. Nevertheless, it is still a fact that BMIs are not just any old bioethical subject matter. This is a technology that enables new discoveries within neuroscience, as well as an unprecedented modulation of our brains. Breakthrough findings regarding fundamental neuronal mechanisms and information processing in neuronal networks are expected in basic research. In addition, miniaturizing the BMIs, bringing the implants towards the nano scale, may take us even further. As a first step, these new BMIs could improve the ability to communicate with individual nerve cells, and may over time even enable us to listen to and interact with the different units within the cell, something unattainable with the current micro sized BMIs.

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4 DARPA, 2009
5 Humanity+, 2009
6 The alarmists, on the one hand, claim that implanting electrodes in the brain could initiate a slippery slope, which ultimately could deprive us of our human dignity or herald a posthuman era that would be the end of humanity as we know it; while the advocates of BMIs, on the other hand, claim that the very same technology could revolutionize medicine, and bring hope of an efficient treatment for a multitude of diseases.
From an ethical perspective, one may ponder whether a deeper understanding of the brain will result in a purely reductionist explanation of consciousness, emotions, behaviour, etcetera, and thereby challenge age old and cemented beliefs and ideas. For instance, what are the implications of such findings when applied to philosophical questions such as free will and determinism; will such fundamental concepts in today’s society as agency and accountability survive? Will the world be disenchanted if, as in recent research, complex phenomena such as morality and religion are explained in terms of neurobiology? Neurophilosopher Patricia Churchland is one of the most prominent proponents of grounding morality and values in evolution, neuroscience, and the trust enhancing hormone oxytocin. Other research, sometimes labelled ‘neurotheology’, searches for God in the brain, or less metaphorically, elaborates on the neural basis of religious experiences. Although these experiments do not necessarily threaten spirituality, researchers such as Sam Harris have suggested that the explanatory powers of this line of research will make religion redundant.

Another set of philosophical queries, those primarily elaborated in this thesis, are posed by the ability of BMIs to interact with, and alter, the brain. BMIs can impact and interact with motor function as well as cognition, emotions and volition, with concrete clinical applications such as allowing a patient with locked-in syndrome to communicate by neural manoeuvring of a computer cursor or to bring a previously treatment refractory depression (TRD) to an end, to mention a few examples. This ability brings us the crux of the matter; BMIs interact with a very special organ, our brains:

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7 Churchland, 2011
8 Newberg, 2010
9 Frank, 2013, p 48
10 Birbaumer, 2006
11 Kennedy, et al., 2011
The brain has a special status in human life that distinguishes it from other organs. Its healthy functioning plays a central role in the operation of our bodies, our capacities for autonomous agency, our conceptions of ourselves and our relationships with others – and thus in our abilities to lead fulfilling lives.\footnote{Nuffield Council on Bioethics, 2013, p xix}

The organ sometimes described as ‘the seat of the soul’\footnote{Churchland, 1996}, gains its prominence since it is “the organ through which the body as a whole is controlled”\footnote{Nuffield Council on Bioethics, 2013, p 73} and, as implied by the metaphor above, the organ that gives rise to our sense of self, to the world of qualia, to cognition, emotions, volition and behaviour – to our unique characteristics as individuals.

The special status of the brain vindicates the ethical imperatives elicited by subjects and patients considered for a BMI. A dysfunctional brain, due to e.g. head trauma or a neurodegenerative disease, can have a profound impact on a person’s life:

The misery and stress of living with a damaged brain, the loss of memory and cognition in dementia, the lack of controlled movement in Parkinson’s disease, the relentlessness of neuropathic pain, and the hopelessness of depression can profoundly change the lives of the individuals affected and those close to them.\footnote{Nuffield Council on Bioethics, 2013, p 13}

The severity of these situations is accentuated by some additional facts about the brain and by our current level of medicine. Even though the brain is plastic, its ability to repair or reproduce damaged tissue is limited. Just a few decades ago it was assumed that a nerve cell once lost, was lost forever. Today we know that there are exceptions to this rule, and that neurogenesis can occur also in adult brains. Nevertheless, most neurons comply with the

\begin{flushleft}
\textit{\footnotesize{12 Nuffield Council on Bioethics, 2013, p xix}}
\textit{\footnotesize{13 Churchland, 1996}}
\textit{\footnotesize{14 Nuffield Council on Bioethics, 2013, p 73}}
\textit{\footnotesize{15 Nuffield Council on Bioethics, 2013, p 13}}
\end{flushleft}
old saying. Moreover, many of the illnesses of the brain are neurodegenerative; they cause an irreversible and progressive loss of nerve cells for which there is currently no cure. Add to this, for instance, the high incidence of major depressive disorder (MDD), Parkinson’s disease (PD), Alzheimer’s disease, spinal cord injury, stroke, etcetera; numbers likely to rise even further as average life expectancy increases.

So were lies the ethical challenge? Considering the suffering caused by these conditions, particularly through impacting our unique characteristics as individuals, displayed in everything from bodily control to personality traits, and the lack of existing effective treatments, one could see why research on BMIs is warranted. However, the sought after advantage of BMIs, to interact with the brain or to alter brain functioning, raises an equally compelling reason for caution. A BMI can impact a person’s inner states and behaviour, raising concerns regarding personal identity, authenticity and autonomy. A BMI can in addition enable neural control of external objects, also over great distances, by thoughts (and the BMI) alone, an ability that for instance raises questions regarding accountability for a BMI-manoeuvred robot proxy. Furthermore with implants that make possible highly controlled and specific brain modulation, and thereby a technological upgrade of our wet, grey innate hardware, mankind can become co-creators of our physical and mental boundaries and abilities. This technology may not only transform medicine, but also the societies we live in, including health, productivity, leisure, morality and religion. Thus BMIs seem to have the potential to alter the alleged nature of the human nature and thereby our present way of life.

16 Nuffield Council on Bioethics, 2013
17 Delgado, 1969
18 Hochberg, et al., 2006
19 DukeMedicine, 2008; Greenemeier, 2008
This thesis originates in a novel ethics project. The project started within an interdisciplinary research group, the Neuronano Research Center (NRC), which develops a new generation of BMIs. The novelty lies in the ethics research actually being situated and conducted side by side with other research, conducted by brain scientists, nanoengineers, data encoders the telemetry unit etcetera, all involved in cutting edge science. Thus, my project stretches the boundaries of traditional applied ethics towards doing ethics as an ‘embedded ethicist’.  

Within NRC we have learnt how to communicate and interact with each other through internal education, journal clubs and weekly lunch meetings. In addition, we have attended the same symposia, workshops and conferences, ranging from the SfN, Society for Neuroscience, gathering tens of thousands of participants, to significantly smaller international expert meetings mixing scientists and ethicists. While other Swedish ethicists study Plato, Kant and Rawls, I’ve been taking courses in neurophysiology, nanotechnology and BMIs, alongside in-depth studies on topics such as unipolar depression and therapies that are possible alternatives to brain implants, e.g. noninvasive BMIs, electroconvulsive therapy and lesioning surgery. As a consequence, I see myself more as a ‘hybrid ethicist’ where ethics is the key component in the analysis, but accompanied with a fair

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20 The term ‘embedded ethicist’ refers to ethicists working in close connection with or as fully integrated members in a research consortium. For a more elaborate explanation, please see the heading ‘Methodological Concerns’.
share of, and an inside perspective on, medicine and technology, or as a bioethicist, though this is not, formally, a thesis in bioethics.

In Sweden, the kind of analysis I am conducting could be undertaken by ethicists, medical ethicists, bioethicists or moral philosophers. These disciplines belong to different faculties, and we all have different training. The ethics unit is based at the Faculty of Theology, where theological ethics and applied ethics have been the major areas of specialization. However, since this is not a typical ethics thesis, some introductory remarks may be necessary. To start with, given the interdisciplinary nature both of the research conducted at NRC at large and in executing the ethics project, the thesis is not only concerned with ethical theory. The objective has never been to develop ethical theory based on abstract reasoning or conceptual analysis alone, but to analyse the specifics and complexities of real life cases and situations combined with a firm scientific perspective. As suggested by the biomedical ethicist Albert Jonsen and the philosopher Stephen Toulmin: in applied ethics conceptual analysis only takes us thus far: “in the end the debate will always return to the particular situation of an individual patient with a specific medical decision”\(^{21}\). Further, the novel contributions in terms of methodology presented in this thesis were mainly developed by necessity, to obtain my objective, rather than being an original goal.

This thesis also breaks another norm regarding theses presented at the Faculty of Theology, at Lund University, since the praxis has been to write monographs. To my knowledge, this is one of the first, possibly the very first,\(^{22}\) compilation thesis presented since the Faculty of Theology, and Lund University, was established in 1666. The particular nature of my project as

\(^{21}\) \(\text{Jonsen & Toulmin, 1988, p 305}\)

\(^{22}\) \(\text{One of the university librarians, Erik Svanström, looked into this matter, and could not find any records of any compilation thesis registered at the Theological Faculty thus far. It is difficult, however, to certify older data since there is always a risk that the digitalized directory may be incomplete. Nor could any of the faculty staff I have talked to recall that there ever has been a compilation thesis presented at the faculty.}\)
well as the general unfamiliarity with compilation theses within ethics is reflected both in the disposition and the content of this text. In light of these particular circumstances, I cannot but agree with an observation made by a fellow Ph.D. candidate a few years back: “[t]he kinds of investigation that form the major part of this thesis do not easily lend themselves to a familiar classification in terms of aims, methods, results”\textsuperscript{23}, and neither, I might add, as depicted in the chapter ‘Philosophical Contexts’, to a conventional overview of previous research. Thus, the logic behind the choices made may not be obvious at a first glance, but will hopefully unfold as we proceed.

Thus, readers should expect an end product very different from a monograph but also different from a compilation thesis in medicine or engineering. Instead of the usual structure, opening with the aim and method of the thesis at hand, I have built a narrative starting in the promises and perils of BMIs, continued by a historic and scientific perspective on brain stimulation together with a highly selective philosophical background, before addressing the actual aim and method. Anyone who prefers a traditional structure should begin by reading the latter sections, as should anyone interested primarily in the ethical concerns addressed, while someone mostly interested in the obtained results can go straight to the two final chapters. For other interests, the table of contents should be sufficient to give reading directions. Moreover, note that the discussion is integrated in the main text, and will therefore not be presented under its own heading.

Besides the structure, there are also other differences from the typical compilation thesis. Aside from the fact that this thesis is lengthier, parts of the research process itself is depicted in some detail. The thesis also aims to initiate a dialogue with the reader, which has been a central concern of my doctoral project; my ambition has been to create a dialogue between both ethics and the sciences, and to present my findings in such a way as to further dialogue between ethicists, scientists and the interested public. Thus, some technical terminology aside, the text is written to be accessible to a

\textsuperscript{23} Broström, 2007, p 28
wider readership. For those not acquainted with medical and technical jargon, a list of abbreviations is included on page 4, whereas key philosophical terms are explained as they appear.

Neuronano Research Center

The NRC was established in 2006 in the first wave of the formation of the Swedish Linnaeus Centres, 20 national Centres of Excellence selected and financed by the Swedish Research Council (Vetenskapsrådet) to support research of the highest quality and strong international competitiveness.24 The NRC initially contained five research platforms or projects:

1) Neural probes
2) Telemetry, data analysis and decision making
3) Neuroscience research
4) Biocompatibility
5) Ethics

These platforms still remain the backbone of NRC, but new competences have been added both within research fields related to clinical disorders, such as depression, pain and epilepsy, and within optogenetics, biomaterials, organic chemistry, pharmacology and neuronanatomy.

In all, roughly 45 researchers from these different areas work towards a common goal, to develop a new generation of BMIs. Thus far, the research conducted at the NRC has resulted in four novel electrodes, all tested in vivo. They range from the first nanowire-based electrode – where each gallium phosphide wire has a diameter of 200 nanometers – to record neural

24 Vetenskapsrådet, 2010
activity in vivo\textsuperscript{25} to a self-anchoring chip electrode\textsuperscript{26} and an electrode consisting of a bundle of ultrathin and flexible microwires, covered in gelatine to facilitate implantation, that unfold once inserted into the brain\textsuperscript{27}.

The key idea behind the electrode designs is that the BMIs are adapted for the specific environment of the brain so that they can remain implanted over long periods of time without causing adverse tissue reactions or deteriorate in function. While there is a long way to go from the current animal studies to clinical practice, the research conducted is guided by NRC’s vision:

\textsuperscript{25} Suyatin, et al., 2013
\textsuperscript{26} Ejserholm, et al., 2011
\textsuperscript{27} Mohammed, et al., 2013
to improve quality of life for disabled people and individuals with neurodegenerative disorders by listening to, understanding and talking to the nervous system by means of a neural interface.\textsuperscript{28}

The ethics project is one of NRC’s five original research platforms. As was described in the grant application to the Swedish Research Council, the main incentive to integrate ethics in to project was that “research on BMI has the potential of establishing a direct contact with the human mind”, and thereby raise a number of ethical concerns. Subsequently, when the NRC announced a vacant position for a doctoral studentship in ethics the stated aim for the ethics project ahead was to study the ethical concerns raised by BMIs, with an emphasis on the BMIs that would be developed within NRC. The specific ethical concerns addressed were to be specified successively and with due consideration to the development within NRC as well as the public debate on BMIs. This objective was the starting point of my doctoral project. Answering to this objective lead to necessary choices on what to include in the analysis, since elaborating on all central ethical concerns raised by BMIs is not a feasible option. Thus, the thesis will address selected ethical concerns elicited by this technology; it is not a review of the ethics of BMIs. Further, though the first paper discusses BMIs in general, the rest of the thesis is focused on DBS.

\textsuperscript{28} NRC, 2013
This chapter gives a scientific introduction to BMIs, containing a note on terminology and the kind of BMIs discussed in the thesis, a historical exposé and an introduction to DBS.

Terminology and Scope

As a first step it is important to make clear what the term BMI refers to. Not all sophisticated implants are BMIs. For instance invasive tracking devices, frequently mentioned in the debate on the surveillance society, are not BMIs since there is no direct communication between the nervous system and the device. The same goes for most prosthetics; only prostheses with a direct communication with the nervous system are classified as BMIs. Currently, there is no authoritative definition, but essentially a BMI can be described as an interface between man (or other animals) and machine created by electrodes – varying in size, shape, number and placement – that are in direct physical contact with the central nervous system. In the literature on BMIs the term has slightly different usages and extensions, and can also be referred to as ‘neuroprosthetics’, ‘neural prosthetics’, ‘direct neural

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29 This historical overview is by no means exhaustive, but nevertheless provides an introductory background to present day brain stimulation.
interfaces’ or ‘brain computer interface (BCI)’. These terms are sometimes used interchangeably, but they can also appear as distinct terms. For instance, the term ‘BCI’ is usually restricted to interfaces involving computers, thus excluding DBS, and ‘neuroprosthetics’ can refer to interfaces linked to peripheral nerves as well as central neurons, whereas BMIs generally are restricted to interfaces with the central nervous system or solely the brain. Since a lack of consensus is a potential source of misunderstandings, some basic distinctions can be helpful.

There are both non-invasive and invasive BMIs. The former do not require surgery, while the latter consist of electrodes directly attached to the nervous system. Implanting an electronic device into the brain involves risks of harm not posed by non-invasive BMIs, but there are also advantages such as a very precise and minute stimulation field or the possibility to obtain neural signals of a higher quality. The latter can be compared with a non-invasive BMI such as EEG that records the brain’s electrical activity by using electrodes placed on the scalp. The neural signals obtained by EEG have important limitations, for instance that they must pass through brain tissue, bone and skin, which diminishes the amplitude of the signals in relation to noise and yields a low spatial resolution, which in turn makes interpretations of the significance of the signals difficult. Hence signals obtained from EEG can currently only be used in comparatively simple applications such as moving a computer screen cursor – a ‘neural cursor’ – or for the neural control of other devices such as a wheelchair.

Another distinction is based on the different directions and subsequent function of the communication between the nervous system and the electrodes; if the electrodes stimulate, and thereby influence, the brain, or if the electrodes are listening to neural activity. DBS is an example of the

30 Lebedev & Nicolelis, 2006; Chase, 2006; Thakor, 2011
31 Lebedev & Nicolelis, 2006, p 536-539; Friehs, et al., 2004, p 2702-2705
32 Chase, 2006, p 228-233
former since the device is used for brain modulation, whereas intelligent prostheses – where the electrodes record neural activity, which is then used to manoeuvre an artificial limb – are examples of the latter. These applications are both examples of one-way communication, though in opposite directions, but other BMIs are aiming at bidirectional communication, in a closed-loop fashion. One such example is the next generation of prostheses that is controlled by the above mentioned principle and additionally – via artificial sensors – send back sensory or positional information to the brain. Another example of bidirectional communication is the electrodes being developed for epilepsy treatment. The BMI monitors the brain’s activity and activates the stimulation only when an upcoming seizure is indicated; thus stopping the seizure beforehand.33

Paper I discusses BMIs in general, but this thesis primarily analyses DBS. As a consequence, BMIs in general are only mentioned in relation to this paper, whereas the rest of the thesis focuses solely on DBS. To be more explicit, from here on non-invasive techniques, either for stimulation of the brain such as repetitive transcranial magnetic stimulation and transcranial direct current stimulation or for listening to the brain such as EEG, will not be discussed. Nor are invasive devices listening to the cerebral cortex, such as electrocorticography, or invasive stimulation electrodes connected to other parts of the nervous system than the brain such as vagus nerve stimulation, phrenic nerve stimulation and spinal cord stimulation included. It is time to close in on DBS.

33 Ackerman, 2006, p 95f
Stimulating the Brain – A Historical Exposé

The medical benefit of electrical stimulation has been known for roughly 2000 years. The Romans used electric fish, such as the black torpedo fish, to alleviate headaches and pain caused by for instance gout and rheumatism. However, it would require some scientific breakthroughs, such as the Leyden jar, lightning rods and the first electric battery, before electrotherapy took the next step. From the 1770s and through the following decades it was suggested that electricity could treat as diverse conditions as epilepsy, paralysis, deafness, blindness, insanity and produce artificial respiration. At the same time Luigi Galvani, closely followed by Alessandro Volta, discovered through experimentation that frog muscles contracted when stimulated by electricity, which showed that electrical stimuli could initiate and modify vital biological functions – without references to metaphysical entities such as ‘vital spirits’.

The experiments continued, and in 1870 the development took one step further with the first experiments on electrical stimulation of the brain in living but anesthetized animals such as rabbits, monkeys and dogs. The German physicians Gustav Fritsch and Eduard Hitzig conducted experiments on canines. By inducing localized body and limb movements they revealed that electrical stimulation of the cerebral cortex can produce movement. By showing that the cortex was excitable they refuted a hypothesis that had been unquestioned since the days of Hippocrates, namely that the brain was a homogenous mass without discrete function.

34 Chase, 2006, p 34f; Fodstad & Hariz, 2007, p 11f
35 Fodstad & Hariz, 2007, p 11
37 Fodstad & Hariz, 2007, p 13
38 Schwalb & Hamani, 2008, p 4
In the 1920s, the Swiss physiologist Walter Rudolf Hess managed to stimulate deep brain structures in unanaesthetised and unrestrained animals. Contrary to occasional claims to that effect, this was not the first successful stimulation of awake animals; a less known German professor named Julius R. Ewald had beat Hess to it in 1896\textsuperscript{39} by walking an implanted dog while its cortex was stimulated by ‘platinum button electrodes’. Hess’ experiments, however, were the first thorough and in-depth studies of their kind. Hess used fine wires to send a current to stimulate deep brain structures in unanaesthetised and unrestrained cats, an achievement that was part of his research on the autonomic nervous system, which later won him the Noble prize in 1949 – a prize which he shared with Egas Moniz, the father of lobotomy.\textsuperscript{40}

In the following years, different kinds of surgically induced lesions paved the way for today’s neurostimulators. Movement disorders were treated with surgical lesions of specific parts of the brain, through procedures like thalamotomy and pallidotomy. In the wake of these surgical therapies the stereotactic frame – which drastically reduced the mortality rates in brain surgery – was developed by neurologist Ernest Spiegel and neurosurgeon Henry Wycis in 1947, followed by a stereotactic atlas of the human brain. These brain surgeries led to increased knowledge regarding the relationships between different movement disorders and specific brain nuclei.\textsuperscript{41} Also electrical stimulation was used in the surgery, to pinpoint where the lesion should be made, since stimulation of the intended structure could help to predict the effect of the lesion and to avoid possible side-effects.

In the 1960s it was discovered that during high frequency stimulation (100 Hz and above) there was a temporary relief of tremor in patients

\textsuperscript{39} Fodstad & Hariz, 2007, p 13f
\textsuperscript{40} Keiper, 2006, p 6-8, 12f; Delgado, 1969, p 70f, 208
\textsuperscript{41} Schwalb & Hamani, 2008, p 4f, 11
undergoing such surgery, and that the symptoms returned when the stimulation ceased. This observation was further elaborated on in the 1980s in research conducted by the French neurosurgeon Alim-Louis Benabid.\textsuperscript{42} In 1987, Benabid showed that high frequency stimulation in the thalamic VIM nucleus had an inhibitory effect on tremor very similar to that of a lesion, a discovery that is often seen as the birth of modern DBS. The implications of this discovery was important; if both techniques could be used for tremor relief, then chronic electrical stimulation could replace surgical ablation, since the former therapy had the advantages – contrary to the latter - of being reversible and adjustable after surgery.\textsuperscript{43}

Early brain implants were not only used to alleviate motor dysfunction, however. Electric stimulation paved way for the discovery of what was termed the brain’s pleasure centre. It was James Olds who during his experiments on rats realized that stimulation of the septum would make the animals neglect primary needs such as food, even when they were hungry. Olds could also control the direction of the rats’ movements through this stimulus. When the rats themselves were given the control of the electric stimulation via a lever, the lever was pressed continuously until the animal was exhausted.\textsuperscript{44} Much subsequent research has been conducted on similar pleasure centres in other animals, humans included.

Experiments on human subjects were conducted by neuroscientist Robert Galbraith Heath from Tulane University in New Orleans, who in the early 1950s was the first researcher to apply a rudimentary form of DBS on

\textsuperscript{42} However, it should be noted that for instance Russian neurophysiologist Nataliya Petrovna Bechtereva already in the 1960s had used bundles of electrodes (24-40 electrodes divided into 4-6 bundles) to stimulate deep brain structures such as the thalamus and the stratiopallidal nucleus for alleviating symptoms in patients with PD, dystonia and phantom limb syndrome; a method she described as therapeutic electrical stimulation and where the therapeutic effects was observable in up to three years. (Bechtereva, et al., 1975)

\textsuperscript{43} Benabid, 2007, p 895; Lyon, 2011, p 331

\textsuperscript{44} Kandel, et al., 2000, p 1009; Keiper, 2006, p 13
humans. The subjects were either mentally or physically impaired, and much of the treatment was based on electrical stimulation of their pleasure centres. The results were striking. Not only could patients with severe depressions experience feelings of contentment during stimulation, stimulating other parts of the person’s brain yielded the opposite response, provoking aggression and rage. Roughly a decade later, Heath conducted an experiment on humans based on the same principle as Olds’ self-stimulating rats. Apparently the participants responded in a similar manner as their rat-predecessors. One man stimulated his brain as much as 1500 times – which forced Heath to abort the experiment, allegedly much to the participant’s dismay.

This very patient was later to participate in one of Heath’s most controversial experiments. The man was homosexual, and had expressed a desire to be heterosexual. Heath saw this as an opportunity to see if conversion of sexual preferences could be achieved by electrical stimulation. Consequently Heath started the experiment by showing the patient stag films while the man’s pleasure centre was stimulated by the implant, which apparently evoked a certain interest for the opposite sex. Heath, however, did not stop at that. Next he hired a female prostitute, with whom the patient

45 However, already in 1874 a physician named Roberts Bartholow conducted experiments on a woman whose skull had been eaten away by cancer. He placed an electrode at different locations on the woman’s cortex and noted how the current could induce subsequent responses in different parts of her body. His place in history seems to have been neglected though, possibly since his experiments initiated seizures that - it was claimed - led the subject to an early grave. (Chase, 2006, p 42f; Schwalb & Hamani, 2008, p 3)

46 Similar experiments were conducted by Carl W. Sem-Jacobsen, a Norwegian physician. From 1952 he used bundles of up to 60-90 micro electrodes placed in deep brain structures both for monitoring and stimulating the adjacent neurons. He reports of over 6500 electrodes used in 136 patients, including experiments on ‘self-stimulation of the positive and negative reward system’. Among the documented responses, Sem-Jacobsen lists acute psychotic episodes, hallucinations, feelings of anxiety, restlessness, depression, fright and horror as well as feelings of ease and relaxation, joy, euphoric laughter, and great satisfaction. (Sem-Jacobsen, 1959)
had intercourse – while the electrodes were stimulating the patient’s brain. Heath consequently concluded that the experiment was a great success, even though it only resulted in a momentary change of the patient’s sexual preferences.47

Another pioneer in the field was the Spanish physiologist José Delgado, a professor in physiology at Yale University. He designed a device he called a stimoceiver, a brain implant with a telemetry system that made brain stimulation possible from a distance, without using connecting wires. In his most famous experiment Delgado allegedly neutralized the aggression in an attacking bull implanted with an electrode for cerebral stimulation. The experiment was set in a bullring, and the bull came charging at Delgado. With only meters left before impact, Delgado activated the implanted stimoceiver thus making the bull abort the attack by merely pressing a button.48

In a similar experiment the stimoceiver neutralized aggression in a dominant male monkey named Ali. The monkey colony Ali belonged to was regularly exposed to his outbursts, but since Ali was the group leader the other monkeys were submissive. Ali immediately retaliated if any monkey tried to challenge the hierarchy. However, when Ali’s caudate nucleus was stimulated, his threatening and aggressive behaviour stopped, and the other monkeys no longer showed any signs of fear for their leader, like maintaining an appropriate distance. In addition, Delgado placed a lever in the cage where the colony lived, a lever connected to Ali’s stimoceiver. Ali’s brain was stimulated whenever the lever was pulled, stopping his bullying behaviour. A female monkey named Elsa quickly realized the connection, and from then on she frequently used the lever to obstruct Ali’s aggressive behaviour.49

47 Keiper, 2006, p 13f
48 Delgado, 1969, p 166-168, 170f
49 Delgado, 1969, p 164-166
Delgado also used the stimoceiver in experiments on human subjects. Severe depression was turned into feelings of contentment, and by stimulating other parts of the patients’ brains other responses such as anxiety, fear and aggression could be triggered, as well as feelings of pleasure, love and affection. Patients could be turned more spontaneous, outspoken and flirtatious, or have their speech processes inhibited. Furthermore, hallucinations could be evoked when the temporal lobe was stimulated. Delgado not only altered mental states, but also induced motor responses. One of these experiments is described by Delgado:

[I]n one of our patients, electrical stimulation of the rostral part of the internal capsule produced head turning and slow displacement of the body to either side with a well-orientated and apparently normal sequence, as if the patient were looking for something. This stimulation was repeated six times on two different days with comparable results. The interesting fact was that the patient considered the evoked activity spontaneous and always offered a reasonable explanation for it. When asked “What are you doing?” the answer were, “I am looking for my slippers,” “I heard a noise,” “I am restless,” and “I was looking under the bed”.

Delgado found these results noteworthy, but was uncertain on how to interpret the responses:

it was difficult to ascertain whether the stimulation had evoked a movement which the patient tried to justify, or if an hallucination had been elicited which subsequently induced the patient to move and to explore the surrounding.

50 Delgado, 1969, p 133-140, 142-149
51 Delgado, 1969, p 150-154
52 Delgado, 1969, p 115f
53 Delgado, 1969, p 116
Another conclusion drawn from Delgado’s experiments is that electrical stimulation overrules will power. If a patient was asked to try to counteract the electrically induced response (referring to both bodily movements and altered mental states), the induced response always took precedence when allowing for a sufficient increase in current.\textsuperscript{54} One of Delgado’s patients commented on this experience when asked to keep his fingers extended during the stimulation – which he failed to do: “I guess, Doctor, that your electricity is stronger than my will.”\textsuperscript{55}

To conclude, a rudimentary form of chronic brain stimulation in human subjects has been used in clinical trials since the 1950s.\textsuperscript{56} The technique had a revival in 1987 when French neurosurgeon Alim-Louis Benabid used high frequency stimulation for symptomatic relief in movement disorders.\textsuperscript{57} Ten years later, the U.S. Food and Drug Administration (FDA) approved the first DBS device for patients with PD and essential tremor. In February 2009, another DBS milestone was reached when the device received a FDA approval – a Humanitarian Device Exemption – to treat a psychiatric disorder: chronic, severe and treatment-resistant obsessive compulsive disorder.\textsuperscript{58} These later studies are not part of an anecdotal past, but are the start of the modern era of brain stimulation.

\begin{flushright}
\begin{footnotesize}
\begin{itemize}
\item Delgado, 1969, p 186f
\item Delgado, 1969, p 114
\item Hariz, et al., 2010; Heath, et al., 1976; Delgado, 1969
\item Benabid, et al., 1987
\item Rabins, et al., 2009
\end{itemize}
\end{footnotesize}
\end{flushright}
Deep Brain Stimulation – A Pacemaker for the Brain

DBS\textsuperscript{59}, sometimes referred to as a neurostimulator or a pacemaker for the brain, is an invasive, chronically implanted device that uses electrical stimulation, where needle-like electrodes stimulate brain structures deep within the brain, like the thalamus or the basal ganglia, in order to alleviate dysfunctions of the brain. Initially, DBS was used as a last resort therapy, as an alternative to lesional neurosurgery, for symptom control in movement disorders such as PD and essential tremor as well as relieving chronic pain. The results were often immediate and striking. Gravely distorted movements changed into close-to-normal movement patterns when stimulation was initiated, and this effect would remain as long as the stimulation lasted. As a result of these drastic improvements in disabling symptoms, more than 100 000\textsuperscript{60} people worldwide currently have DBS implants in their brains.

In clinical practice today, DBS is primarily employed to improve motor function in conditions such as PD, essential tremor and dystonia. Conversely, there is extensive ongoing research to evaluate additional brain targets as well as new indications such as:

\textsuperscript{59} The following text is to a large extent a duplicate of my technical description of DBS in article IV.

\textsuperscript{60} These numbers only include patients with a Medtronic DBS system for PD, essential tremor, and dystonia, so the total number is higher. (Medtronic, 2013)
Current DBS systems consist of three parts: a lead, the extension cable and a pulse generator. The pulse generator is usually placed beneath the collar bone. It resembles a cardiac pacemaker, and produces electrical pulses that pass along a wire, the extension cable, to the lead, which is implanted into the brain. The patient usually has two leads, one in each hemisphere. The

61 Holtzheimer, et al., 2012; Kennedy, et al., 2011
62 Fisher, et al., 2010
63 Patel, et al., 2011
64 Lipsman, et al., 2013
65 Hamani, et al., 2008
66 Schiff, et al., 2007
67 Smith, et al., 2012
68 Anderson & Kartha, 2013
69 Keiper, 2006, p 19
70 Franzini, et al., 2012
most common lead is a very thin device, 1.27 mm in diameter, with four cylindrical electrode contacts close to the tip.

Figs 2 & 3. The DBS system is presented to the left and the lead with the four electrode contacts to the right. (Photo: Rehncrona)

The electrode contacts can be activated and altered individually to control the stimulation field. The effect of the stimulation is fine-tuned by adjusting the general settings of the pulse generator such as amplitude, frequency and pulse width. A physician or a specially educated nurse programs the general settings, but the patient can usually make minor adjustments such as switching the device on and off, or changing the voltage within pre-set
limits by communicating with the pulse generator via a magnet. Consequently, the therapeutic effect, as well as stimulation related adverse effects, is adjustable after surgery. In addition, the stimulation — and hence the effects on the brain — can be terminated either by switching off the pulse generator, or if required, by removing the implant from the brain.\footnote{Johnson, et al., 2008}

DBS procedures are performed at specialized medical centres and require extensive preoperative preparations. Candidates for DBS surgery must be thoroughly assessed, and be judged suitable by a mixed board of health care professionals,\footnote{In Sweden this board consists of 2 neurosurgeons, 2 neurologists and a PD nurse} before they are accepted. The surgery may last for four to seven hours, including the time for magnetic resonance imaging and requires meticulous intra operative planning. Advanced imaging techniques together with stereotaxy, where a stereotactic frame fixed to the head provides three-dimensional coordinates to pin-point the target area where the lead should be placed, direct the positioning and placement of the lead. The patient is usually\footnote{One exception to this rule is the DBS surgery undertaken at the University Hospital of Umeå, Sweden, where the implantation now, without negative impact on the outcome, by routine is made under general anesthesia. (Fytagoridis, et al., 2013), p 70} awake during surgery, since ensuring that the electrodes ends up in the right place is in part based on the effects observed in, and communicated by, the patient. Some surgeons also use recording microelectrodes to direct the placement of the lead by monitoring surrounding nerve cell activity.\footnote{Medtronic, 2002} The placement of the lead, i.e. the brain area or nucleus intended for stimulation, depends on the indication and displayed symptoms as well as individual differences between patients, such as the occurrence of comorbidities. The targets for stimulation are subcortical brain structures such as the subthalamic nucleus, the internal

\footnote{Johnson, et al., 2008} \footnote{Medtronic, 2002} \footnote{In Sweden this board consists of 2 neurosurgeons, 2 neurologists and a PD nurse} \footnote{One exception to this rule is the DBS surgery undertaken at the University Hospital of Umeå, Sweden, where the implantation now, without negative impact on the outcome, by routine is made under general anesthesia. (Fytagoridis, et al., 2013), p 70} \footnote{Medtronic, 2002}
globus pallidus, the ventral intermediate thalamic nucleus or the nucleus accumbens.

Positioning the lead is not an easy procedure. Some nuclei, such as the subthalamic nucleus, are minute, while others, such as the peripeduncular nucleus, are rather complex, which sometimes means that the position of the lead needs to be corrected later on. In addition to the neurosurgery, the pulse generator and extension cables are also surgically implanted. DBS also requires extensive postoperative care. Patients have to return for additional
check-ups and repeated visits to adjust the settings of the pulse generator in order to find the best outcome regarding therapeutic benefits and minimizing adverse effects. Replacement of the pulse generator is required when the battery is depleted; a roughly 20 minute surgery under local anesthesia. Moreover, managing hardware malfunctioning also requires specialist care. Thus, undergoing DBS creates long term dependency on specialist care. All in all, this makes DBS an expensive, time-consuming and specialist dependent procedure.

Furthermore, although DBS is life changing for some, the procedure is not without problems. Complications can occur due to the surgery, the hardware or the stimulation. The surgery poses immediate risks of harm such as hemorrhage, infections, and skin erosion. Implanting the DBS device in the brain can also result in adverse effects such as dysphagia, swollen eye and pain. Furthermore, the surgery can pose long term risks of seizures, personality changes and weight gain, etcetera, as has been observed after surgically induced lesions. Malfunctioning hardware is another concern. Both mechanical and electrical complications such as lead fracture or migration, malfunctioning or depleted batteries, or unintended external interference with the device that impacts on function do occur. Then there are the stimulation induced complications, for instance cognitive and mood

76 Rabins, et al., 2009
77 Yet, DBS can still be considered a cost-effective treatment when taking into account the costs of PD drugs, absenteeism from work etc. For further reading, see (Dams, et al., 2013; McIntosh, 2011)
78 The price varies, but in Sweden the cost is in rough numbers SEK 200 000, equaled to just above € 20 000; while Medtronic estimates the cost for a bilateral implantation as $50,000 to $60,000, including the cost of the device as well as hospital and physician’s fees. (Schwalb & Hamani, 2008), p 11
79 Bewernick, et al., 2010
80 Sachdev & Sachdev, 2005
81 Okun, et al., 2005
associated changes such as speech impairments, confusion, depression or mania, hypomania (hypersexuality, compulsive gambling, etc.), mirthful laughter, pseudobulbar crying, aggression, personality disorder, apathy, anxiety, irritability, and obsessive and suicidal behaviour. In addition, there have been anecdotal reports of enhanced memory and creativity due to the stimulation. The adverse effects resulting from the stimulation can often be eliminated or at least reduced by changing the stimulation parameters, but there are also cases when a sufficient therapeutic response is only obtainable with stimulation parameters that also evoke adverse effects.

Aside from these concerns, there are additional reasons why DBS therapy may sometimes not be successful. First of all, the preoperative screening may have been inadequate, for instance not detecting contraindications that speak against a successful outcome, such as comorbidities or age. Equally important is that the device is correctly programmed, usually requiring four to eight adjustments in the first six months alone. In a screening of PD patients with suboptimal outcome of their DBS treatment, 15 out of 41 patients improved significantly after adjusting the stimulation parameters. In addition, there are both structural

82 Benabid, 2007; Lyon, 2011
83 Juckel, et al., 2009
84 Demetriades, et al., 2011
85 Okun, et al., 2003, p 28
86 Hamani, et al., 2008
87 President’s Council on Bioethics, 2004
88 Okun, et al., 2005
89 Harries, et al., 2012
90 Bell, et al., 2009, p 3
91 Okun, et al., 2005
and functional differences between individual brains. Thus, two patients with leads in the same position and the same stimulation parameters can still not expect the same treatment outcomes.\textsuperscript{92} Also, the individual brain may change due to its plastic capacity, so the outcome of DBS, both regarding therapeutic response and adverse effects is difficult to predict exactly (including long term outcomes), and may vary from patient to patient. In addition, it is not uncommon that the therapy results in the sought-after medical improvement, but that the patient still finds the outcome problematic. This tendency may be related to unrealistic expectations; troubles adjusting to the new situation such as no longer receiving that special care and attention from significant others or to find a new way of life after years of disabling symptoms; or feelings of estrangement and alienation toward one’s own person after the procedure, to no longer recognize oneself.

However, modifications are underway to increase the therapeutic effect and avoid some of the shortcomings in today's DBS usage and technology. These modifications can either be realized by new uses of or by refining the current DBS technology, or consist in mergers with other methods. In order to localize the stimulation with a significantly higher degree of accuracy than with bilateral leads there have been trials with 3D stimulation, where five leads were positioned to target the same brain nucleus, amounting to ten leads and 40 electrodes in total for both hemispheres.\textsuperscript{93} The adjustability thereby achieved is a means to increase the therapeutic effect and reduce stimulation related side effects.

A higher degree of control over the outcome of the stimulation can also be achieved by developing electrodes designed for the intended brain structure or to downsize the current technology, possibly ending up with nano-sized electrodes.\textsuperscript{94} Yet another example of new electrode design is non-

\textsuperscript{92} Rabins, et al., 2009

\textsuperscript{93} Benabid, 2007

\textsuperscript{94} Suyatin, et al., 2013; Benabid, 2007
rectilinear leads\textsuperscript{95} or ultrathin flexible bundle electrodes. The former lead is characterized by its bent shape, while the latter is a multichannel neural probe with several ultrathin leads that unfold once inside the tissue, where, besides improvements in biocompatibility, a selection of the miniaturized leads can enhance specificity and reduce side effects.\textsuperscript{96}

More radical transformations of DBS technology are also underway, such as a closed-loop real-time device that both listens to and stimulates the brain. The operational principle of this device is that the implant monitors the patient’s neural activity, and that the stimulation is triggered only when specific neural changes are detected. These bidirectional implants have been tested for epileptic

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\textsuperscript{95} Benabid, 2008

\textsuperscript{96} Mohammed, et al., 2013
patients,\footnote{Morrell, 2011} and the first successful use in patients with PD has been reported.\footnote{Santos, et al., 2011} Another signal of this development was the Medtronic Inc, the leading DBS manufacturer, launch of a bidirectional system in August 2013.\footnote{Medtronic, 2013} Additionally, for instance optogenetics, where light of specific wavelengths is used to impact individual cell types within the brain, could be a possible candidate for a merger with DBS, a hybrid that due to its ability to control individual cells has the potential to transform the future of brain modulation.\footnote{Gradinaru, et al., 2009; Thakor, 2011}
This chapter introduces the philosophical background to and framework for the ethical analysis conducted. Due to the particular nature of my project, the research undertaken has touched on a wide variety of subjects. This also explains why the chapter has the heading ‘Philosophical Contexts’ as opposed to ‘context’ in the singular. The issues encountered can roughly be divided into three main headings: biomedical ethics, science and technology ethics and classical ethical concerns. Under these headings some of the highlighted topics have been nanoethics, implant ethics, neuroethics, autonomy, authenticity, personal identity, resource allocation and distribution (both locally and globally), brain modulation for psychiatric disorders and enhancement, and radical future perspectives including cyborgs, Humanity 2.0 and Grey Goo. It is not necessary to recapitulate all these topics here, especially since quite a few of these discourses turned out to be less relevant for my project when not only the subject matter, but also the approach to doing ethics, was taken into account.

The main reason for ending up with this diverse mix of philosophical subjects is the novelty of brain implants. If the subject matter for ethical analysis is cutting edge science there tends to be little or close to no previous research against which to position yourself or use as a starting point for further reflection. Thus one has, by necessity, to look for adjacent ethical concerns to find an adequate theoretical framework. Or in the words of Jonsen and Toulmin: “the first substantive task is to agree just which basic

\[\text{EGE, 2005; Hansson, 2005}\]
‘paradigm’ best fits the circumstances in question”.¹⁰² I started with an orientation¹⁰³ within neuroethics, nanoethics and ethical concerns elicited by implants in the human body, to get an overview of were the key ethical concerns relevant for BMIs might be found. As the project progressed and my specific research questions were formulated and addressed, new subjects were encountered and integrated into this analysis.

As this chapter unfolds, the philosophical terminology and scope is presented, and some of the philosophical contexts encountered depicted. The latter includes a discussion of the contemporary debate when my project was initiated, largely a story of lacunas, as a background to my first choice of enquiry. Moreover, I introduce and elaborate on the prime ethical concern discussed in my papers: ethical perspectives on the personality changes that have been reported in some patients after undergoing DBS. In all, this philosophical background is highly selective but still representative, since it depicts the possibilities and problems in targeting cutting edge research as well as in applying classical ethical issues such as personal identity over time and authenticity to the frontiers of science.

Terminology and Scope

Most philosophical terms used in this thesis will, when necessary, be defined as they are introduced. The only terms that need to be explained at present are ‘ethical concerns’ and ‘bioethical concerns’. Unless the opposite is clearly stated, these terms are used interchangeably throughout the thesis. I do not suggest that all ethical concerns are bioethical concerns, but the kind of ethical concerns elaborated on in this thesis are, unless something else is stated, bioethical ones. Further, by an ethical ‘concern’ I refer to ‘a matter

¹⁰² Jonsen & Toulmin, 1988, p 308
¹⁰³ Ethics and BMIs – Mapping the field, unpublished manuscript. (Johansson, 2007)
for consideration’. Within bioethics the term ‘ethical concern’ is commonly used as a synonym for something ethically problematic, for moral threats. This is, as just stated, not the intended use of the term in this dissertation. To assess a technology or a scientific breakthrough, possibilities as well as risks must be given due consideration for a balanced ethical evaluation. I therefore use the terms ‘ethical concerns’ or ‘bioethical concerns’ without a presupposed evaluative content.

The scope in terms of the ethical analysis and content must also be made explicit. As stated in the second chapter, this thesis will only incorporate a selected few of all the possible ethical concerns one could address regarding BMIs. Leaving BMIs in general behind after the first paper, and subsequently only focusing on DBS, does not suffice to avoid this selection process. I refer to the chapter ‘Aim and Method’ for an explicit description of the particular concerns put under scrutiny. Though as a general remark, the content of this thesis tends to be shaped more by my approach to doing ethics than a specific subject matter or discourse within ethics.

It is also important to clarify the thesis’ relation to normativity. A common expectation is that an ethical analysis should result in some sort of recommendation on how to act, i.e. to conclude whether an action is morally prohibited, permitted or required. The predominant way of doing bioethics is based on top down reasoning, where standard normative theories, such as utilitarianism or contractualism, or for instance the Georgetown mantra, are applied to the object of analysis, so called ‘principle-based approaches’. This way of doing bioethics, both with regards to the means

104 Rachels, 2001, p 15

105 The four principles of autonomy, nonmaleficence, beneficence and justice, introduced in the seminal work Principles of Biomedical Ethics. (Beauchamp & Childress, 2009) However, Beauchamp and Childress themselves explicitly express the deliberation of these principles. Thereby they exhibit a less obvious connection to pure principle-based reasoning than how the principles commonly are employed.

106 Childress, 2001, p 61ff
and the end, differs from the kind of analysis I am conducting here. Thus, someone who prefers a principle-based analysis or seeks an overall verdict on the ‘to be or not to be question’ of DBS will have to look elsewhere. This, however, is not to say that moral reasoning based on principles have no place in bioethics, nor that the thesis makes no normative claims; evaluative content is in a strict sense impossible to avoid. Further, I do employ the mid-level principles\textsuperscript{107} derived from my bottom up analysis. Yet my main undertaking is to identify, critically assess and problematize central ethical concerns rather than to provide their answer.

The First Discussions on Ethics and DBS

By 2007\textsuperscript{108} there was plenty of scientific literature on DBS, but discussions on the ethical implications were scarce. This fact was emphasized in a review on print media coverage of neurostimulation techniques in the USA and the UK published that year by Racine et al. Of the examined articles only 14\% included a discussion on ethics – which could be compared to articles on genetics or genomics where ethical issues are present in close to 40\%.\textsuperscript{109} A search in Lund University’s electronic library information navigator – containing more than 15000 e-journals and 500 databases – in

\textsuperscript{107} Rachels, 2001, p 16f

\textsuperscript{108} To my knowledge, the first big controversy on brain stimulation occurred in the 1970s. Books such as José Delgado’s \textit{Physical Control of the Mind: Toward a Psychocivilized Society} and \textit{Violence and the Brain} by neurosurgeon Vernon Mark and psychiatrist Frank Ervin, sparked a debate on mind control and political incentives for psychosurgery. Media coverage and congressional hearings lead to a drastic decline of the field. Another big controversy emerged when the cochlear implants were introduced. Since cochlear implants are not DBS, that ethical debate will not be discussed here, but there is much written on the subject elsewhere, for instance (Lane & Grodin, 1997; Davis, 1997; Glover, 2006)

\textsuperscript{109} Racine, et al., 2007, p 314
November 2008 supported Racine’s findings;\textsuperscript{110} the search on DBS rendered 2304 articles, whereas a search on DBS and ethics rendered 12, i.e. less than one per cent.\textsuperscript{111} The current situation does not show a marked increase in attention to ethical issues; the same search five years later rendered 30 027 total results, out of which 399, or 1.3 per cent, considered ethical issues.\textsuperscript{112}

Considering the general objective of this thesis, early writings on DBS and ethics available tended to be either too broad, with DBS mentioned as one example among many within larger contexts like neuroethics, implant ethics or the ethics of neurosurgery,\textsuperscript{113} or too specific, focusing, for example, on patients with PD dementia or selection procedures for patients.\textsuperscript{114} The problem with the former approach is that the analysis of the ethical implications specifically addressing DBS tended to be rather superficial, if at all undertaken. The problem with the latter approach is that the specific ethical concerns elaborated may have little to do with one’s own research objectives. I will exemplify this below.

In 2005 the European Group on Ethics of Science and New Technologies published a report, \textit{Ethical aspects of ICT implants in the human body}. This report on information and communication technology implants was extensive in relation to other publications on ethical aspects of implants in the human body. The main devices mentioned, summarized below, are\textsuperscript{115}:

\begin{itemize}
\item \textsuperscript{110} Note that these numbers only give a rough comparison, since the Racine study examined the content of the articles where my search only reveal the number of hits generated.
\item \textsuperscript{111} Retrieved on Nov 4\textsuperscript{th}, 2008
\item \textsuperscript{112} Retrieved on Nov 8\textsuperscript{th}, 2013
\item \textsuperscript{113} EGE, 2005; Hansson, 2005, p 519-525
\item \textsuperscript{114} Farris, et al., 2008; Bramstedt & Ford, 2006, p 161-164
\item \textsuperscript{115} EGE, 2005, p 7-12
\end{itemize}
• Medical devices
  o Cochlear implants and Auditory Brainstem Implant (ABI)
  o Implantable programmable drug delivery pumps
  o Implantable Neurostimulation Devices
  o Deep Brain Stimulation (DBS)

• Identification and location devices
  o RFID devices (Radio frequency identification, used for livestock, pets, laboratory animals, and endangered-species identification.)
  o Medical records and healthcare information (blood type, potential allergies and medical history)
  o Personal information/identity
  o Financial information (secondary verification)

• Surveillance or tracking devices
  o Wearable ICT devices for tracking the human body

• Enhancement or commodity devices (future possibilities)
  o Artificial hippocampus
  o Artificial vision (infrared)

As shown by this overview, the range of implants included is vast, but the ethical discussion focused on an analysis of information and communication technology implants in general, even within the different subcategories. Except for a section listing circumstances calling for special caution, there among “implants that influence, determine or change psychic functions” and “implants influencing the nervous system and particularly the brain and thus
human identity as a species as well as individual subjectivity and autonomy”,116 there was nothing in the ethical analysis that addressed ethical concerns specific for DBS, even though the technique was mentioned.

My second example illustrates the opposite case: very specific discussions on DBS and ethics, but on concerns rather far from those with which I am concerned. One of the first ethical concerns raised regarding DBS was informed consent. In a 2006 paper, two challenges regarding informed consent were identified. The first challenge addressed the patient’s ability to fully understand and elaborate on risks such as personality changes, cognitive decline or loss of memory; especially considering that the indication at hand, with neurological dysfunction as the common denominator, also may impair the patient’s capacity to make decisions:117

Since the problems corrected by functional neurosurgery involve the central nervous system, and the central nervous system influences the way people think, evaluating a patient’s capacity to make decisions can be difficult. […] this becomes even trickier when the potential risks involve psychological impairment or cognitive loss as well as motor or sensory loss. The psychological state of a patient who has functional impairments, especially chronic pain, can make a robust informed consent process challenging.118

The second challenge concerns the patient’s right to revoke a given consent to undergo DBS and participate in a trial. There have been cases when a patient revokes consent during the DBS surgery and wants to abort the procedure immediately. This situation can occur since most patients are awake during the DBS surgery, i.e. when the electrodes are inserted into the brain. The question is whether it should be perceived as a genuine revocation of consent, or as a request mostly influenced by a temporary feeling of anxiety caused by this highly unusual, and, regardless of the sedatives,

116 EGE, 2005, p 26
117 Ford & Henderson, 2006, p 216, 220
118 Ford & Henderson, 2006, p 220
probably rather unpleasant situation. In addition, the surgeon can only terminate the surgery if it is safe to do so; otherwise the patient’s request will be declined. There have been suggestions to use so called ‘Ulysses contracts’, where the patients sign a form before surgery, where they give up their right to withdraw consent; but such contracts are controversial both from an ethical and legal point of view.\footnote{Ford & Henderson, 2006, p 220f}

This was just two examples of the problems involved in finding adequate research that could further my own research interests. Nanoethics at that time seemed absorbed by nanoparticles, futuristic scenarios and defining itself as a new discipline within applied ethics. Conversely, neuroethics was preoccupied by research on pharmaceutical enhancements of cognition, mood, etcetera, alongside a growing interest in brain imaging and a field of study sometimes called ‘neuroscience of ethics’, the study of the neural underpinnings of behaviour, morality, and religious experiences. However, the debate on enhancement touched on one concern that seemed highly relevant for an ethical analysis of DBS, ethical perspectives on DBS induced personality changes.

**Personality Changes and DBS**

One of the central ethical concerns raised by DBS, and the principal concern addressed in this thesis, is the occasional occurrence of non-transient personality changes. Before addressing these ethical concerns, some conceptual clarifications are required. First, the term ‘personality changes’ has distinct meanings not only within psychiatry, psychology and philosophy, but usually also within different fractions of these disciplines. For instance, while in a clinical setting a change must be rather substantial to count as a personality change, it is not necessarily so in the philosophical
discourse, since in that context there are different bids as to what should be considered a ‘personality change’. I will apply a pragmatic view of the term, since my key interest is to critically examine the kind of changes actually brought about by DBS, and on what grounds these changes can be considered to be ethically problematic – or, depending on the premises at hand, as is argued in paper III, desirable.

However, first some additional clarifications. The kind of changes here included under the label ‘personality changes’, do not necessarily refer to ethically equivalent concepts of change. When considering an ethical evaluation of DBS, this variety of labels and contents may obscure the analysis. For instance, patients who after DBS claim that they “feel like someone else”, are with all likelihood not referring to actually having turned into a different person, though the latter would be the conclusion for someone making the same claim from the theoretical framework of personal identity over time. Consequently, it does not suffice to take the terms \textit{de facto} used in the debate at face value, without also considering what they (actually) refer to. For instance, changes in behaviour, personality and personhood, are changes of very different prominence from an ethical perspective. One can experience changes in behaviour without having a changed personality. Conversely, someone’s personality may change, though this individual would still be one and the same person. Below I will elaborate on how these changes, through different philosophical frameworks, can – or cannot – provide insights to the analysis of DBS. The latter is important as I am not interested in evaluating the philosophical theories discussed in general, only according to their usefulness in analysing DBS. Also, in the subsequent use of the term ‘personality changes’, I include all these different interpretations lest something else is specified.

It is important to acknowledge that changes in personality are not ethically problematic per se. Many changes are considered admirable and sought-after, such as becoming kinder, wiser, and more conscientious. During the course of a human life people indisputably change, in ways both subtle and blatant, gradually or overnight. It is interesting to note that also in psychiatry, there seems to be a shift towards acknowledging personality traits as less static. While the definition of personality traits according to the American Psychiatric Association’s \textit{Diagnostic and Statistical Manual of Mental Disorders}, DSM-IV, was “enduring patterns of perceiving, relating to, and thinking about the environment and oneself that are exhibited in a
wide range of social and personal contexts”. The definition in DSM-5 is “a tendency to behave, feel, perceive, and think in relatively consistent ways across time and across situations in which the trait may manifest.” Thus ‘enduring patterns’ have been replaced by ‘a tendency’ and ‘relatively consistent’.

When analysing DBS, there are some key aspects related to personality changes that must be taken into account. First, some of the impairments that necessitate the DBS intervention in the first place, be it motoric or cognitive dysfunction, may result in changes in personality. These changes become apparent when PD deters a former athlete from training or when a philosophy professor loses her analytical ability and eloquent way of expressing herself due to a severe depression. Second, some medications, such as L-dopa for PD patients, may cause side effects such as hypomania or drowsiness; side effects that may well be considered as a change in personality. Third, there are changes brought about by treatment, both symptom relief and adverse effects. The patient, or her significant others or physician respectively, may either affirm or find these changes troublesome. Thus, a comprehensive discussion on personality changes as regards DBS cannot be reduced to a question merely of non-transient adverse effects brought about by DBS.

With this introduction, we can return to the earlier claim that personality changes is one of the central concerns raised by DBS. To justify this claim, we need to recapitulate the argument made in the first chapter. From an ethical perspective, there is one crucial difference in research on brain modulation techniques such as DBS and other medical research: the brain has a special status. In the 2007 report *Intervening in the Brain: Changing Psyche and Society*, the Europäische Akademie describes the brain as the “organ of the mind”, and continues:

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120 APA, 2000, p 686
121 APA, 2013, p 772
As such it is widely held to be the origin of mankind’s unique position among living beings. Likewise, on the level of the individual human being, the brain is considered the material substrate of those traits that in combination render each person unique.\textsuperscript{122}

The brain enables the mind, and the mind enables the subjective notion of “the self” or “you”. Thus, a technology that alters the brain can, through this capacity, alter the mind and all those traits that constitute this self, i.e. our unique characteristics, our personalities. This capacity seemingly calls for special ethical attention.

It is important to note that these ethical concerns are not unique to DBS; they have been voiced regarding for instance neurosurgery in general as well as in “psychosurgery”, the treatment of psychiatric disorders through surgical incisions such as lobotomies; electroconvulsve therapy; psychopharmacology and sometimes psychotherapy.\textsuperscript{123} Thus, the common denominator is the capacity, \textit{mutatis mutandis},\textsuperscript{124} to impact the constituting elements of our (sense of) self, although there are claims that new brain modulation techniques “may transform patients in more radical or profound ways than more established techniques of intervention”\textsuperscript{125}. In light of these potential alterations, it seems necessary to consider what changes to a person’s self that matter from an ethical perspective or, in other words, determine what alterations are arguably ethically problematic and why.

\textsuperscript{122} Europäische Akademie, 2007, Preface

\textsuperscript{123} Fink, 1999; Europäische Akademie, 2007, p 189

\textsuperscript{124} Each intervention has characteristics that impact the way the brain is modulated and the possible adverse effects. Some of the key characteristics of DBS are that the therapy requires brain surgery; that the implants are intended to remain in the brain, often until the patient’s death; that the treatment is reversible, the currents can be stopped or the device explanted; that the stimulation is adjustable after the surgery; and that this technique is spatially and temporally specific, giving a higher precision to the outcome.

\textsuperscript{125} Europäische Akademie, 2007, p 386
A common approach to this question has been to examine if personality changes elicited by DBS can threaten personal identity. This matter, together with concerns regarding enhancement, was for instance the main philosophical concern addressed in *Intervening in the Brain: Changing Psyche and Society*. Another example surfaced at a conference on the ethical implications on brain modulation techniques I recently attended, where one of the keynote speakers argued that numerical identity is a suitable theory for analysing such changes. Few would dispute that, if DBS indeed poses a threat to personal identity over time, this would be very severe from an ethical point of view. If, that is, DBS really does or can cause alterations so radical as to support the claim that the person about to undergo this treatment would turn into a different person as a consequence of the intervention. Note that this claim is conditional. There are, however, as I will show below, both conceptual and practical reasons to question the usefulness of analysing the personality changes elicited by DBS by employing theories on personal identity over time.

For instance, as noted by the Dutch philosopher Maartje Schermer, for philosophers who advocate a biological view of numerical identity, it is

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126 In short, “What makes a person at one time and a person at some another time one and the same person?” (DeGrazia, 2005, p 13) sometimes referred to as the reidentification question. The questions of personal identity over time gains its importance since it deals with so called continuants, the persistence of a single entity that maintains its existence over time despite undergoing changes. However, where is the breaking point? What would it take, i.e. what kind of changes are required, to claim that a person before and after such a change is no longer one and the same person; that the old person has ceased to exist – replaced by a new person?


128 Usually these arguments take off by quoting DBS patients who pronounced that they no longer recognize themselves, or that they feel like someone else. However, I sincerely doubt that these patients are referring to a state of being equivalent to the strict criteria for no longer being the same person according to the philosophical views on numerical identity. This is but one example why conceptual clarifications are required to elaborate on the thorny concerns regarding personality changes and DBS.
conceptually impossible that alterations of the brain caused by DBS, even drastic alterations, could pose a threat to numerical identity. The biological view(s) is based on bodily continuity, i.e. the persistence of (a sufficient amount of) body and brain. Thus, since DBS does not threaten bodily continuity, using this position as an analytical tool will not take us far. Do the view that psychological continuity is what determines numerical identity fare better than the biological view in addressing personality changes caused by DBS? Only a tad. Let us recapitulate what kind of alterations DBS de facto have caused: speech impairments, confusion, depression or mania, hypomania (hypersexuality, compulsive gambling, etc.), mirthful laughter, pseudobulbar crying, aggression, personality disorder, apathy, anxiety, irritability, obsessive and suicidal behaviour, as well as anecdotal reports of enhanced memory and creativity.

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129 Schermer, 2009, p 46
130 DeGrazia, 2005, p 13f, 21
131 In addition, one should not forget that the occurrence of side effects are dependent on what nuclei that is being stimulated, where the subthalamic nucleus stands out, that some of these side effects are very rare, and most importantly, that many are transient or could be avoided by changing the stimulation settings.
132 Benabid, 2007; Lyon, 2011
133 Juckel, et al., 2009
134 Demetriades, et al., 2011
135 Okun, et al., 2003, p 28
136 Hamani, et al., 2008
137 President’s Council on Bioethics, 2004
According to the psychological view(s), what matters for personal identity is sameness or continuity of mental life, where overlapping memories usually is a necessary (and sometimes sufficient) criterion for persistence over time. However, a person may experience drastic personality changes without memory being completely disrupted; thus, according to most versions of the psychological view of numerical identity, the person would still be one and the same after such alterations. Consequently, if the aim is to find a fitting theory to critically elaborate on the above mentioned side effects of DBS, the psychological view of numerical identity over time seems insufficient. In comparison to the biological view, it is, however, still possible – if highly unlikely – that psychological continuity could be terminated by DBS, i.e. where the person after DBS by definition is another person than the person existing before the procedure, since the necessary criteria for personal identity to be sustained are no longer fulfilled.

The main argument made by the Europäische Akademie has similar limitations. They build their argument around a set of criteria for being a person, e.g. based on, depending of the version at hand, specific elementary cognitive, emotive and motivational states and abilities, as well as having a body. Thus, that personhood will persist is what matters for personal identity to be maintained. Other changes that may occur during the course of a lifetime, and whether these changes are brought about by DBS or by encountering for instance new experiences and values are irrelevant according to this account. By what factual criteria would DBS pose a threat to personal identity according to this view? The following conclusion is presented: “a change of personal identity evoked by an intervention in the brain would have to manifest itself as a dissociative disorder, e.g. retrograde amnesia or dissociative identity disorder.” Later, however, a remark is made that there currently is no evidence that any such threats to personal identity are

138 DeGrazia, 2005, p 14, 20f
139 Europäische Akademie, 2007, p 386
identity are likely with regard to the techniques, DBS included, evaluated. Therefore, also this approach seems insufficient to address the known complications of DBS.

Given these examples, the question of personal identity does not appear as the most suitable candidate to elaborate on the kind of personality changes that DBS actually can and does bring about. So, to return to the previously made conditional claim: if DBS poses a threat to personal identity this would be very troubling from an ethical perspective, but this does not seem to be the case given the use of DBS to date. In addition, there are practical considerations here that cannot be neglected:

if there was a higher than negligible risk for patients undergoing a particular kind of intervention to be bereft of necessary capabilities for being regarded as persons, then the procedure in question would not be employed.

Thus, early in the report the Europäische Akademie states the conditions under which a therapy will not be undertaken, but they nevertheless choose an analytical tool that only detects those very same radical changes.

Before proceeding, a final remark on personal identity is in place. The conclusions on the limited usefulness of personal identity as an analytical tool to elaborate on the personality changes brought about by DBS here presented are drawn with regards to the current use of DBS, and the upcoming upgrades to this technology presented in the thesis. Though in line with the central message in paper IV, and in accordance with the aim to reflect also on future concerns, with changing technology ethical concerns

\[\text{140} \] For a refutation of DBS as a threat to personal identity when understood in terms of narrative identity, I refer to (Baylis, 2011)

\[\text{141} \] Europäische Akademie, 2007

\[\text{142} \] To make sense of such restrictions, it is important to remember that DBS is employed to alleviate disabling symptoms and thereby increase quality of life. DBS is not curative, nor is it a lifesaving intervention. Thus, the acceptable risks of harm in DBS are not comparable to cases where an intervention can be the difference between life and death.
may both arise and be overcome. Thus, there is always the possibility that future developments and applications of DBS will give us reasons to reconsider personal identity as a key ethical concern. To address the current situation, however, we have to look elsewhere to find ethically challenging cases where the answers are less obvious; therefore I chose a different analytical framework.

As apparent primarily in paper III and IV, I decided to use authenticity as a theoretical framework to approach the personality changes elicited by DBS. The philosophical term ‘authenticity’ cannot be used without further specification. A thorough introduction to the entire cluster of core ideas, assumptions, normative claims and genealogy connected to the term is not possible within the current scope, but a few remarks and conceptual clarifications are necessary. In addition, I should mention that it was with great hesitation I finally settled for authenticity, considering that I find some of the claims, both metaphysical and normative ones, associated with this term problematic.

One suggestion on how authenticity differs from theories on numerical identity over time comes from the Dutch philosopher Felicitas Kraemer. She proposes that while theories on personal identity focus on criteria for numerical identity over time, “the key-question of authenticity is which of the different ‘selves’ can count as the ‘real’ one, i.e. the true self.”143 Though this is a very common understanding of authenticity, I nevertheless find it problematic. Determining what self that is the ‘true’ self is an epistemic concern, based on the ontological assumption that there is such a thing as a true self in the first place. Personally I do not, at present, have a cemented view on the nature of the self, apart from rejecting the static views affirming an unchanging self and also being somewhat sceptical of the idea of a self that is “constantly shifting and reacting and altering”.144 More importantly, I

143 Kraemer, 2011, footnote 3
144 Williams, 2002
suggest that these concerns are set aside. The relevant concerns are the normative features of authenticity, to elaborate on authenticity as a value. This approach is not different from the approach that allows us to discuss the value ascribed to religious beliefs without first having to clarify whether or not there is a god. Since adding a metaphysical claim regarding a ‘true’ self adds nothing of value to the discussion, but does bring about a lot of problems, it seems better not using it at all.

Thus, as I see it, the strength in employing authenticity as a theoretical framework to approach personality changes caused by DBS lies in elaborating on the (ethical) implications of common interpretations of this term in the literature; with the aim to discern what we have good reason to take into consideration and where, on the other hand, voiced concerns are uninformed or oversimplified. One example of the latter is discussed in paper III, such as claiming that DBS can be a threat to the value of authenticity since the intervention aims to alter cognition, mood, and behaviour, without taking into account the changes to cognition, mood, and behaviour caused by the disorder, thus already impacting the patient’s authenticity. Another claim that is challenged is that the aim of DBS should be to restore a premorbid self, an aim relying on a view of the self as a constant, not impacted by years of living with a severely disabling condition or other important life events. Thus, authenticity as a heuristic tool can reveal incoherent arguments based on adjacent assumptions regarding personality changes in the debate on ethical DBS.

Another set of problematic arguments, although a slight detour from personality changes, is based on two common additaments to authenticity – ideas of ‘naturalness’ and ‘artificiality’. It is not unusual to encounter arguments claiming that “an artificial means necessarily leads to an inauthentic result”, 145 and that an inauthentic result, in turn, is ethically problematic. Regarding medical interventions, this position is hard to defend. According to such accounts causation is prior to the outcome of the

145 Kraemer, 2011
intervention, and thereby the ethically decisive feature. Though, a DBS intervention, and other medical therapies, do not easily comply with this categorization. Still, I hypothesize that ideas of naturalness and artificiality may be the more or less pronounced premises in arguments claiming that impacting the brain is ethically problematic, or, that a brain implant by default is ethically problematic in virtue of being an artefact situated in the brain; something highly “unnatural”. For instance, the technology bias identified and discussed in paper II is an example of this line of reasoning. As shown in paper II, scientific facts and analogies with adjacent ethical considerations can help to identify and avoid such biases.

Finally, the notion of authenticity seems suitable for addressing some of the concerns or reflections voiced both by prospective and implanted DBS users. Empirical research can help to pinpoint what patients refer to when expressing “I no longer feel like myself”, “I feel like a robot”\textsuperscript{146} or, the PD patient explaining that she after receiving DBS experienced “a third version of me,” in comparison to the version […] prior to Parkinson’s Disease and the version affected by the disease but prior to the effective symptom relief provided by DBS\textsuperscript{147}. These concerns are discussed in paper III and IV, but I nevertheless want to give some opening reflections on the topic here.

For some patients, these reported changes in self-perception were perceived as deeply problematic, while other patients did not report experiencing any such changes, or, conversely, that the changes experienced were not considered as problematic. Accordingly, for some patients the authenticity could be considered an important value, but for others less so. Here directed research could be beneficial for improving the information to prospective DBS candidates. Consequently, to capture the subjective experience of (perceived) personality changes, there is a need for a theoretical framework to make sense of and elaborate on these reported

\textsuperscript{146} Schüpbach, et al., 2006
\textsuperscript{147} Johansson, et al., 2011
experiences.\textsuperscript{148} For this perspective, theories on narrative identity can also provide important input. However, to include also the perspective of the patient’s significant others and health care team, authenticity, devoid of the previously mentioned ballast, may be a candidate for that job.

\textsuperscript{148} Kraemer, 2011
This chapter presents the aim of the thesis, how the general objective of NRC’s Ethics project was turned into specified and manageable research questions, and the method used to address them. First, the rationale for the choices made will be made explicit, followed by a discussion of methodology and how the attempt to overcome some methodological challenges resulted in the approach used in this thesis – ‘embedded ethics’.

The general objective of the NRC’s Ethics project was to address the ethical concerns raised by emerging BMI technologies, with an emphasis on the research conducted within NRC. The specific ethical concerns addressed within the project were to be specified successively and with due consideration of the development within NRC as well as the public debate on BMIs. The aims of the thesis as a whole are formulated to answer to the general research objective. One aim is to discern and elaborate on urgent and prominent concerns elicited by BMIs developed at the NRC. Further, I strive to critically evaluate arguments relevant to an ethical analysis of DBS, such as identifying potential biases in the ethical evaluation of DBS, and to scrutinize arguments addressing ethical concerns elicited by current, upcoming and future DBS technology. Finally, I aim to address and develop ignored or underrepresented perspectives of importance in an ethical analysis of DBS. I will return to these overarching aims in the two concluding chapters. Next the specific research questions addressed in the individual papers will be introduced.
The Process of Formulating Specific Research Questions

Although this section partially overlaps with the penultimate chapter, the two sections have distinct objectives. This section presents the rationale for selecting the specific research questions addressed in the thesis. The chapter ‘Papers I-IV: Summary and Main Conclusions’, in contrast, describes the key novel contributions and main conclusions of the papers. Including a section that depicts the research process and not only the results, may seem peculiar. However, since my specific research questions were to be specified successively, with due consideration to the contemporary ethics and DBS debate as well as the outcome of the research questions I had addressed thus far, the logic behind the choices made may seem random lest this process is made explicit. Moreover, given an approach aiming for a higher degree of specificity in conjunction with an increasing knowledge of the subject matter, it is not surprising that the first two papers address a cluster of questions, whereas the later papers have only one specific objective.

Undertaking an ethical analysis of cutting edge research has its pros and cons. When approaching the very frontiers of science, it is, due to the lack of previous contributions, not too difficult to answer up to the novelty requirement. Since so little has been written, most contributions add something new to the debate. However, these very lacunas are also an obstacle. As shown above, the lack of relevant literature and well-established perspectives made the choice of the first area of inquiry difficult. Where does one begin an analysis of the ethical concerns that arise from the development and implementation of nano and micro scaled multi-channel electrodes for both stimulation and recording purposes? Before deciding, I wrote a review mapping three areas of potential interest in an ethical analysis of BMIs: Neuroethics, nanoethics and ethical concerns in relation to implants in the human body.149 Among these three areas, the choice finally

149 Johansson, 2007
fell on nanoethics. Nanoethical concerns had to be considered since NRC’s electrodes involved nanotechnology, and such concerns had reached the public debate through questions of risk assessment and precautionary measures.

In paper I, I entered the nanoethics discourse by asking whether any new ethical considerations are raised if nanotechnology is added to current BMIs, and, whether an analysis of the particular topic of BMIs can shed new light on the emerging field of ‘nanoethics’? The rationale for the first objective was to determine whether the most urgent ethical concerns were raised by the use of nanotechnology, or, in the actual interface between the nervous system and an electronic device. Further, I hoped to make a contribution to the emerging field of nanoethics at large. The conclusions, in short, were that nanotechnology has an enabling potential, and can elicit some additional ethical concerns, but that the main ethical challenges seemed to arise by using BMIs *per se*. With regards to the nanoethics discourse I argued, with BMIs as the example, that the field suffered from a number of severe teething troubles. For instance, many contributions put too much emphasis on generalizations and speculative future scenarios, as well as arguing about the actual need of nanoethics as a subfield within ethics, instead of addressing the ethical challenges raised by nanotechnology – regardless of how this enterprise is labelled or whether the questions posed are unique or not.

One of the main conclusions drawn from working on paper I was the need to be specific regarding the subject matter of ethical enquiry. It seemed impossible to say something substantial on ethical concerns when grasping for too much, as, for example, is the case with an attempt to make an ethical analysis covering everything from implants to free floating nanoparticles, nanomedicine to antibacterial socks, current applications and science fiction scenarios like Grey Goo. This conclusion led to the realization that trying to analyse BMIs in general was equally troublesome. Another realization was the importance of balance in the subjects covered by the analysis, to spot the lacunas. Within nanoethics, many have had their eyes either on future scenarios or debating the status of nanoethics as such, while the most imminent concerns have garnered considerably less attention.

Therefore I decided to close in on DBS. DBS raised urgent ethical concern since this was a BMI already in clinical use, and especially since the
use of these pacemakers for the brain were expected to increase drastically.\textsuperscript{150} However, it soon became obvious that DBS in general was also too diverse a subject for an in-depth ethical analysis since there seemed to be ethically relevant differences regarding DBS in clinical practice and in research targeting new indications; between motoric and psychiatric DBS; current applications versus the prospect of using DBS for enhancement purposes, etcetera. To overcome this diversity, paper II closed in on DBS for one sole indication, unipolar TRD. One reason why the choice fell on psychiatric DBS was the historic stigma associated with the use of brain surgery for treating psychiatric disorders. The (mis)use of lobotomies and other surgical lesions to treat psychiatric disorders, so called psychosurgery, is a crude reminder of what can happen if a promising technique (as previously mentioned Egas Moniz, the father of lobotomy, did receive a Nobel prize in 1949 for introducing this therapy) is spread prematurely and without caution.

I hypothesized that some arguments regarding TRD DBS could be impacted by the historic stigma associated with psychosurgery, together with fictional accounts of psychiatry such as the blockbuster \textit{One Flew Over the Cuckoo's Nest}, and campaigns against current treatments within psychiatry staged by for instance the anti-psychiatry movement and Scientology. Therefore, a key objective was to separate fact from prejudice, and more specifically, to examine if there were undetected biases both in the scientific and public debate that could impact an ethical evaluation of TRD DBS and public perception of this therapy, including affecting prospective patients. However, to obtain a balanced analysis, I also wanted to investigate if the opposite preconception occurred, i.e. overly positive accounts regarding TRD DBS.

Another reason for choosing psychiatric DBS was that the goal of this treatment is to alter thoughts, emotions, behaviours and volition distorted by the disorder, features closely linked to a patient’s personality and core

\textsuperscript{150} Decision Resources, Inc., 2006, figure 3
characteristics. At face value, psychiatric DBS seemed more problematic from an ethical point of view than motoric DBS, since the former corrects distorted minds and the latter distorted movement. Choosing one indication alone, TRD DBS, followed from my emphasis on specificity. Further, it was a response to the ethics publications at that time, where most contributions analyzing psychiatric DBS treated these indications as a group instead of targeting individual indications. Thus, one of my objectives became to discern the ethical concerns specific for DBS for unipolar TRD as opposed to psychiatric DBS in general on the one hand, and alternative measures for this particular group of patients on the other.

That the choice of indication was unipolar depression also has its reasons. This is the most common psychiatric disorder worldwide, affecting more than 150 million people at any given time. Since 10–20% of the patients diagnosed with MDD\(^\text{151}\) do not respond the conventional treatment, the number of patients that can potentially be considered for TRD DBS are considerable. In addition, MDD is a potentially deadly disorder; among severely affected patients, one in six commits suicide.\(^\text{152}\)

After finishing paper II, it became obvious that specificity regarding the DBS technology and the indication at hand was not enough. Brevity is necessary when writing papers for peer reviewed journals, and when starting on paper III, I had finally realized that specificity is equally important with regard to the ethical concerns analysed. While still addressing DBS for depression, I closed in on one ethical concern – authenticity. I was troubled by the fallacies occurring in some arguments on DBS and personality changes, so I addressed these arguments by elaborating on the implications of promoting a value of authenticity. The aim of this paper was to show what made these arguments problematic. This inquiry, together with the insights gained by working on paper II, pointed to yet another conclusion. DBS’s

\(^{151}\) Lozano, et al., 2008; Shields, et al., 2008

\(^{152}\) Malhi & Bartlett, 2000
ability to impact cognition, volition, emotions and behaviour arguably requires special attention in an ethical analysis, but due to our neuroanatomical wiring the crucial concern seems not to be whether the target indication is psychiatric or motoric DBS, but rather what the actual outcome of the brain stimulation *may* be. Thus, these concerns are by no means limited to psychiatric DBS. As a part of this realization, the divide between psychiatric and motoric DBS seemed less relevant, so paper III marked the end of my focus on psychiatric DBS.

When writing paper IV I therefore opted for a new take on the ethical evaluation of DBS. There had been some papers addressing “the ethical future of DBS”, but these papers primarily discussed DBS for novel indications or DBS enhancement. One important consideration had been overlooked: how a developing DBS technology can impact future ethical concerns. Currently identified ethical challenges of DBS are subjected to change. This may seem like a trivial observation, but one that nonetheless has very important implications. If an ethical analysis only discusses current ethical concern, it may soon become dated. Therefore, discerning potential changes to the present concerns can provide an idea of what ethical concerns that can be expected in the years to come. Of course every attempt to make predictions of future ethical concerns must be undertaken with caution, but to ignore future challenges altogether is an even less appealing alternative. Thus, addressing this particular lacuna was the specific objective in paper IV.
Methodological Concerns

The method used in this thesis differs from the dominant principle-based approach within bioethics\(^{153}\) on more than one account. The method here described is the outcome of trying to find a functional way to do bioethics that would conform to the outlined premises of my doctoral project. Thus, after a somewhat tentative beginning, I came to develop and employ a method that I refer to as ‘embedded ethics’\(^{154}\), which builds on some of the tenets of empirical ethics and, as I will return to below, casuistry. Empirical ethics, the outcome of the so-called ‘empirical turn’ of ethics emerging in the past decades, are by no means a unified approach to doing ethics. The term encompasses such diverse approaches as using empirical methods to study morality,\(^{155}\) to new ways to undertake philosophy of technology. Dutch philosopher Philip Brey has characterized the latter, the approach relevant here, as ‘a family of approaches to technology and its social significance that is more concrete, more empirically informed, more constructivist and less pessimistic about technology’\(^{156}\). This new framework could be seen as a response to critiques of mainstream bioethics being:

- too abstract, too general, too speculative, and too dogmatic, as well as too far removed from clinical reality, insensitive to the peculiarities of specific situations, and unable to adequately consider the nature of diseases and the clinical contexts\(^{157}\)

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\(^{153}\) Childress, 2001, p 61  
\(^{154}\) I am not the first to use the term ‘embedded ethics’. I will elaborate on the different ways this term have been used below.  
\(^{155}\) Borry, et al., 2004, p 1  
\(^{156}\) Brey, 2010, p 40  
\(^{157}\) Borry, et al., 2004, p 2
Accordingly, the Dutch philosopher Albert Musschenga argues that “the ultimate aim of all empirical ethics is to improve the context-sensitivity of ethics”. I was not aware of this diversity within empirical ethics when I started my doctoral project; at that time I had mainly encountered the branch doing empirical studies of morality such as the experiments conducted by US social psychologist Jonathan Haidt and experimentalist Joshua Greene. Otherwise, this theoretical framework would have suited my undertakings. Even so, to some extent, the mentioned characteristics of empirical ethics seem to validate my own method, as will be shown in the last part of this chapter.

To proceed, we must make clear what we refer to when talking about “doing ethics”. First, one might refer to the actual role of the ethicist. Second, one might refer to the ethical method chosen in the analysis being conducted. This distinction is important, and I will use it to illustrate the difference between the ‘embedded ethicist’ and ‘embedded ethics’. Especially among Dutch philosophers, there has in the last couple of years been an ongoing discussion of new ways of doing ethics in the former sense, where both terms such as ‘embedded ethicists’ and ‘parallel ethicists’ have been introduced. The difference between the embedded and the parallel ethicist, according to van Gorp et al., is that “the embedded ethicist cooperated more closely with the researchers”, but the approaches used are similar. Thus, it seems reasonable to focus on characterizing these approaches and to downplay the role of the actual labels.

The Dutch approaches have been characterized by ethicists working alongside other researchers while the actual research, i.e. subject matter for ethical analysis, is initiated and executed. The degree of involvement has

\[\text{158 Musschenga, 2005, p 468}\]
\[\text{159 In empirical ethics, the same ambiguity is present with regards to the use of the term 'method', and, equally, I use the term in the twofold sense in this heading.}\]
\[\text{160 Gorp & Molen, 2011, p 32}\]
ranged from ethicists only linked to the project to, more rarely, those integrated in a research consortium from the start and remaining a part of the group for the duration of the project. The importance of the latter was emphasized; all relevant ethical concerns could not be identified beforehand, for instance in the project application, but became apparent only as the research progressed. In this particular sense my role at the NRC has been embedded.

It is important to reflect on the pros and cons of being embedded. The advantage of working as an embedded ethicist is that it throws you right into the actual circumstances and contextual settings of your subject matter. Thus, the ethical concerns identified are shaped by a thorough familiarity with the technology. Naive ethical concerns based on ignorance or unfounded assumptions are consequently more easily avoided. Analysing a brain modulation technique like DBS requires both an understanding of how the brain works – and maybe even more importantly, does not work – and the potential and bottlenecks of the technology as such. As I have argued elsewhere, this is a responsibility resting on any ethicist taking their analysis seriously. It is highly problematic to criticize or praise a technology without first familiarizing yourself with that technology and its usage. Another advantage of being embedded is the possibility to be proactive. By integrating ethics from scratch, the ethical evaluation can have an actual impact on the development and outcome of the project at hand. It enables an ethical “look before you leap” strategy, and simultaneously provides the other involved researchers with new perspectives on their own ethical reflections.

However, the inside perspective also comes with risks. Some worries are voiced in the literature. For instance, being part of, and often paid by, a consortium may discourage the ethicist from being open with his opinions

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161 Gorp & Molen, 2011, p 42
162 Johansson, 2011, p 127
and especially potential criticism of the research. Another concern is if the ethicist becomes so integrated in the project that the critical distance is lost, and for that reason becomes too affirmative.\textsuperscript{163} A similar concern has been voiced from social scientists, claiming that ethicists lack the adequate methodological competence for handling the inside perspective. From my personal perspective, I believe that such concerns are likely to vary from case to case, and rely on factors such as the integrity of the parties involved, how the research is conducted, whether the other parties also seek an ethical development or are primarily looking for the “good press” resulting from having an ethicist on-board. Van Gorp describes their experiences as unproblematic,\textsuperscript{164} though there is no guarantee that all embedded ethicists will have similarly experiences.\textsuperscript{165}

The other way of understanding ‘doing ethics’ refers to the method used when conducting the actual ethical analysis. It is in this sense I use the term ‘embedded ethics’. Thus, this specific use of the term should not be confused with “the undertaking of an embedded ethicist”, as seems to be the most common usage to date.\textsuperscript{166} In the next section, the key features of this approach are introduced.

Before proceeding, some limitations must also be discussed. Since developing a method to address my research questions was not an original aim of this thesis, I have not done any explicit research on methodology per se. This clearly poses a severe constraint to the claims presently made. Directed research is required before a more elaborate theory of embedded

\textsuperscript{163} Gorp & Molen, 2011, p 41

\textsuperscript{164} Gorp & Molen, 2011

\textsuperscript{165} Here methods used within other academic disciplines, such as action research, insider research and practitioner research, could provide valuable input.

\textsuperscript{166} The term ’embedded ethics’ has also been used to describe ’ethical practices’ that do occur in a specific group or organization. However, this is a study of ethics (in practice), not in ethics; and thus a usage of the term ’embedded ethics’ very far from the one presented in this thesis. (Gordon, et al., 2009 )
ethics as a method of ethical enquiry can be presented, and also to discern its relation to methods already used within other fields of study. Still, even if an elaborate account of necessary and sufficient conditions defining embedded ethics will have to wait until this research has been undertaken, the general outlines can and will be provided below. Despite these current limitations, the method has proved its usefulness by producing the novel contributions presented in the thesis. However, as a consequence of this method being developed as my research progressed, it is only in the later articles that it has been fully implemented. Although the key components can be spotted already in my first papers, they have successively become more pronounced and refined as I have learnt from others as well as my own mistakes.

Embedded Ethics

Below I will describe the theoretical framework I ended up with in my attempt to address my specific research questions. As previously stated, a main difference between embedded ethics and principle-based approaches is that the former uses a bottom-up or case-based approach in ethical reasoning. The bottom-up approach is well-known within ethics, used in for instance casuistry where analysis and classification of particular cases and circumstances are used as a base for a general account of ethics.167

There is disagreement on whether a bottom-up approach can stand alone in an ethical analysis, or must be supported by or interacting with top-down approaches. However, the relevance of this issue is closely related to the claims of the approach employed – to what extent the outcome of the analysis is intended to be action guiding, i.e. to provide normative guidelines, or not.168 Since determining whether or not specific actions are

167 Jonsen & Toulmin, 1988, p 11
168 Arras, 2001, p 109
right or wrong is not, as previously stated, the aim of embedded ethics, I do not, for the present purpose, need to address this issue. For our purpose, it suffices to clarify that a bottom-up approach should here be understood as undertaking moral reasoning starting in the particulars of the subject matter, acknowledging and incorporating the complexity of reality, with all its nuances and details, and elucidating relevant contexts and analogies, to discern central ethical concerns.

Two building blocks of embedded ethics have now been introduced: moral reasoning based on a bottom-up approach, with the objective to identify, outline and problematize central ethical concerns, rather than to provide specific guidelines on what to do. Moreover, embedded ethics requires three additional features: specificity, familiarity and contextual considerations. As with all analytical tools, when applied, the boundaries between categories are seldom absolute, but that does not mean that categorization cannot be used. These additional features will now be exemplified with the subject matters of this thesis.

Specificity: This feature secures precision in the analysis. Both the subject matter to be analysed and the number of ethical concerns possible to include considering the format given, must be adequately specified. This demand is a clear demarcation against all attempts to talk about technology in singular form, i.e. giving little or no attention to differences between technologies or, to detailed study of concrete technological practices, artefacts or processes.169 Here, part of the nanoethics debate is a striking example, also when talking about subcategories such as nanomedicine, or the European Group of Ethics’ report on information and communication technology implants as discussed in the chapter on philosophical context.

Familiarity: Embedded ethics requires a thorough familiarity with the subject matter of analysis. The ethicist has to acquire a sufficiently firm and comprehensive knowledge of the science, technology or research area at

169 Brey, 2010, p 39
hand to obtain this inside perspective. Being an embedded ethicist is one way of acquiring this perspective. This perspective is also common within bioethics, among for instance doctors and nurses doing research in medical ethics, or engineers doing research on ethics and technology, sustainability etcetera. Alternatively, a thorough familiarity with for instance genetic testing or brain imaging, if those are the subject of ethical analysis, can be obtained by means other than working within these fields of science. The decisive feature is rather to be knowledgeable enough to be able to detect and incorporate relevant nuances and details in the ethical analysis as well as to recognize arguments that may be philosophically coherent, but lack scientific feasibility.¹⁷⁰

**Contextual considerations:** This heading entails quite a few different types of concerns. A method only focusing on specificity runs the risk of losing the bigger picture, and the bigger picture usually entails features important for the particulars. Technology does not exist in a vacuum; it is situated. For instance, in order to analyse DBS one must consider its actual placement in the brain, and the continuous development of the implants over time. Another important concern addresses potential alternatives, such as ablative surgery or new medications. It is not possible to assess pros and cons without considering the pros and cons of other options. If an effective non-invasive therapy were to become available, then brain surgery will become superfluous. Focusing on the context gives an overview of the kind of ethical concerns that are being discussed. Ignored or underrepresented perspectives can thereby be identified. Some considerations are attention grabbers and as the first chapter suggested, brain implants raise many such issues. Some may seem pressing, but are they really, all things considered? Rephrased, is there a reasonable balance in the ethical concern addressed, or do some issues steal all the thunder? Such imbalances may impact the overall perception and evaluation of DBS and must therefore be heeded, for

¹⁷⁰ I’m not referring to thought experiments here, but attempts to do applied ethics without assuring that one has the facts straight.
instance if the analysis primarily focuses on ethical problems without taking into account the advantages.

These are the key elements of the method *de facto* used in the thesis. By combining specificity, familiarity and contextual considerations one can discern the concerns that ought to be considered in any ethical analysis of DBS. Further, by emphasizing the dependencies that impact and interact in an ethical analysis of DBS, by bringing in analogies with similar ethical concerns, concerns that seem intuitively important and urgent can be critically examined.
PAPER I-IV: SUMMARY AND MAIN CONCLUSIONS

As a general remark, the papers here presented were written over a six-year period. I started my Ph.D. studies in June 2007, and wrote the manuscript for paper I during that first summer. Paper IV was written in the last year, and submitted in mid-2013. Some of my ideas have changed during this time span, as has – I hope – my ability to analyse the ideas with which I am concerned. A recurrent feature in my two first papers is the attempt to cover not only the actual subject matter, but also related questions and perspectives. Providing different angles to the chief ethical concerns seemed like a good idea at the time, but I would have chosen differently today. In this chapter I will not recapitulate all the perspectives discussed in the individual papers. Instead this summary will bring forth the key points, the central novel contributions and main conclusions of the papers. It is thereby also shown how the results obtained from the papers fulfil the aims of the thesis.

Paper I: Brain-Machine Interfaces and Nanoethics

Paper I addresses the intersection of BMIs, nanotechnology and nanoethics. It was written to address a few frequently occurring themes in the emerging field of nanoethics. Thus, the overarching aim was to show why these themes are problematic, and at the same time to analyse the ethical implications of BMIs from a nanoethical perspective. After introducing and discussing the first problematic theme in nanoethics, generalizations, i.e. sweeping ethical statements that fail to do justice to the great diversity within nanotechnology, I suggest that a relevant and substantial ethical analysis of nanotechnology requires a high degree of specificity regarding
the subject matter. Therefore, I limit the analysis to BMIs and argue that this subject matter also requires further specifications as a prerequisite for in-depth ethical analysis. Two key questions are then formulated and targeted: are any new ethical considerations raised if nanotechnology is added to current BMIs and can analysis of the particular topic of BMIs shed new light on the emerging field of ‘nanoethics’?

The results in short include identifying key ethical challenges raised by BMIs, namely issues of health hazards/safety, autonomy, authenticity, identity, privacy, justice and equity, and well-being. The ethical challenges raised by BMIs based on nanostructured microelectrodes as well as nanoelectrodes are then identified and discussed. The key ethical concern that emerges when fusing nanotechnology and BMIs is safety, including evaluating the appropriate level of precautionary measures required to tackle the safety risks. However, this and other concerns such as justice, obtaining informed consent when facing expected unknowns, difficulties regarding patents and intellectual property rights, are already raised by the use of BMIs as such. Thus, they can at most add an extra dimension to concerns already present due to the interface between man and machine per se.

For instance, in clinical applications, using nano scaled electrodes may be an overkill, considering the fact that the size of neurons’ cell bodies are micro scaled, and that microelectrodes therefore probably are sufficient for an effective BMI. However, microelectrodes with nanostructured surfaces might help to improve durability, biocompatibility and recording/stimulation characteristics. Instead, the new benefits of nano scaled BMIs are anticipated within basic science. These electrodes can open up for the possibility not only to listen to and interact with individual cells, but also to different units within the cells. If so, these BMIs could provide ground breaking insights into how the brain works, thus possibly impacting our self-concept as human beings. This, in turn, may raise new or at least additional ethical concerns.

Then there are the results from the second question, whether an ethical analysis of a particular subject matter, BMIs, can shed new light on the emerging field of ‘nanoethics’. More specifically, I use the analysis of BMIs as a means to illustrate why some of the most common topics or approaches within nanoethics up until 2007 were problematic. Regarding generalizations I argue that (useful) normative guidelines cannot incorporate and handle the entire scope of nanotechnological applications. For instance, there are
significant differences between a nanostructured implant in the brain and exposure to free floating nano particles. In addition, there may be ethically relevant differences between electrodes made of nano wires and nanostructured microelectrodes, and whether the device stimulates the brain or records neural activity. If all nano applications are bundled together, relevant ethical differences may pass unnoticed, and specific applications may thereby unjustly be judged as more promising or dangerous than they actually are.

The next series of concerns addressed are somewhat different. These concerns are not problems per se, but become problematic if they are emphasized at the expense of other, more urgent, concerns. As a means to determine the relative importance of an ethical concern I propose a model to distinguish the urgency of a concern based on the timeframe, degree of threat, and probability. Using this model, the predominant focus on distant futures and ‘speculative ethics’ is criticized. With ‘speculative ethics’, I refer to the use of this term suggested by the philosopher Alfred Nordmann, namely when a hypothetical scenario, usually involving farfetched and highly improbable nanotechnological applications available in a distant future, through a subtle leap, is treated and described as a technology that is imminent and factual, and therefore a valid concern when evaluating current research. Thus, ‘speculative ethics’ should not be confused with thought experiments at large. The latter can be a useful philosophical tool, whereas the former arguments are flawed. It is a fallacy to argue for a ban or boost of current nanotechnological development without acknowledging if the technology described is highly speculative, scientifically feasible, or already present. While speculative ethics should be avoided altogether, a one-sided emphasis on discussing distant-future technologies is still problematic. Despite the striking nature of the latter technologies, it is more urgent to address the nanoethical concerns that are raised by current and imminent nanotechnological applications. Thus, I call for a more balanced coverage in the nanoethics debate, so that science fiction does not steal all the thunder.

The final criticism is directed at another question that has received considerable attention in the nanoethical debate, namely if the novelty of ethical concerns should be the criterion to justify nanoethics as a subdiscipline in its own right? Although classifications and conceptual clarity is essential in philosophy, I argue that this cannot be all there is,
especially in applied ethics. My main point is that the question of whether there is need for a specific subfield within ethics labelled ‘nanoethics’ is secondary to addressing the actual ethical concerns raised by the increasing use of nanotechnology. In addition, I challenge and problematize the claim that to justify the emergence of a new subfield, nanotechnology must give rise to completely new ethical concerns.

**Paper II: DBS for Treatment Refractory Depression**

Paper II discusses DBS for TRD. This was one of the first papers to focus specifically on TRD DBS instead of discussing psychiatric DBS in general, and was, when published, the most comprehensive paper on the subject matter. One objective was to identify both the ethical concerns specific to DBS for unipolar TRD as opposed to psychiatric DBS in general and the available alternatives to experimental DBS for this particular group of patients. The comparison was made by employing the bioethical principles of beneficence and nonmaleficence. Further, in response to the first published paper on DBS and MDD, we argue that there may not be many ethical concerns unique to DBS for TRD and that the relevant question is what concerns that are specific for TRD DBS, as opposed to claims of uniqueness.

The other main objective of paper II was to identify and create an awareness of potential biases in the ethical evaluation of DBS. As a part of this analysis, we both identify and discuss biases that can impact the results in studies on TRD DBS, for instance time, as well as overly simplified and polarized views on DBS for TRD, here depicted as blind optimism and unfounded fears. These biases raise ethical concerns and are mediated – sometimes unintentionally or through misunderstandings – by, for example, scientists, ethicists, media, internet or fiction. From a patient perspective, exposing these biases is imperative. Patients will not benefit if a promising treatment is avoided due to unfounded fears, nor will they benefit if DBS is used without scrutinizing the arguments that call for caution.

One of the paper’s novel contributions is to identify and elaborate why time is a crucial concern in TRD DBS. Apart from the frequent mentioning of the necessity of regular follow-ups after the DBS surgery, up until 2010,
when paper II was written, concerns related to time were scarce. Still, time concerns are essential when assessing the efficiency of TRD DBS. Time could, literally speaking, be a matter of life and death. We argue that if the efficiency of DBS is measured solely by the numbers achieved from standardized depression rating scales at a predefined point in time; much of the story is left untold. Depression is a potentially deadly disorder, so a quick therapeutic response can be lifesaving. Thus, if the objective is to act in accordance with the principle of beneficence, a crucial consideration is how long it takes before the therapeutic response (partial and full respectively) is obtained. Another crucial point is the duration of the obtained therapeutic effect. In the first study published on TRD DBS, four out of six patients were responders one week after the operation and one of these four patients was in remission. Hence, an early onset of the therapeutic effects was obtained. But were the results lasting throughout the entire trial? No. The effects fluctuated during the six months follow up period. In addition, one of the initial non-responders needed two months before responding to DBS, but was by the last follow up one of two patients in remission. Similar fluctuations in the depression rating scores have been present in later studies as well.

While TRD DBS is still in the research phase, proper means of evaluation are necessary to judge whether there is a rationale to employ DBS on a larger scale. Thus, in light of these fluctuations, it is important to pose the question whether time could become a bias in this assessment. Measuring the outcome of a study in terms of the results on depression scales obtained at one occasion alone, i.e. the last follow up, could be viewed as a kind of bias, since the duration and stability of this particular result is left out. Furthermore, another potential bias is that these numbers say very little on what has happened with the depression in practice. Is there a general reduction of symptoms, or have some symptoms been drastically reduced while others appear unaffected? Consequently, to act in accordance with the principle of beneficence our means of assessing the obtained results of DBS for TRD must be satisfactory. This may not be achieved with today’s measurements alone.

Another novel contribution is to identify and elaborate on potential technology biases, the assumption that implants – in terms of their invasiveness and size (in comparison to pharmaceuticals or say plasticity) – are ethically problematic *per se*. Through specificity, both in terms of a
detailed account of the relevant scientific concerns and ethical considerations, it can be revealed if praises of, or objections to, DBS for TRD seem adequate given how equivalent ethical concerns are evaluated. Among the features to be specified are the disorder at hand, i.e. chronic, severe and treatment-resistant depression, and the proposed therapy, i.e. what has been achieved with DBS as a therapy for MDD, including the technique’s advantages and limits. For instance, an argument is not coherent if DBS’s ability to directly influence the brain is considered to be ethically problematic, whereas other comparable means to directly influence the brain, such as pharmacotherapy, transcranial magnetic stimulation, or simply drinking too much, are not, mutatis mutandis, considered to be (equally) ethically problematic.

Thus, the most important contributions of this paper are to introduce the actual ethical challenges facing TRD DBS, and to identify some of the existing biases that an ethical evaluation on TRD DBS must be aware of.

Paper III: Authenticity, Depression and DBS

Paper III returns to DBS for TRD. Its novel contribution was to critically evaluate arguments based on the value of authenticity that had appeared in some papers on ethical DBS. The aim of paper III was to show what made these arguments problematic. The notion of authenticity is frequently merged with normative assumptions, and a common outcome of this (unholy) alliance is the claim that it is morally problematic to diverge from who we really are, i.e. something of value is lost if we fail to be authentic. Conversely, we are considered to be less authentic if we fail to express some part of our defining characteristics in our daily lives, such as relationships, professional life, and hobbies. The main problematic argument addressed is the sometimes implicit, sometimes explicit, claim that DBS can be a threat to the value of authenticity since cognition, mood, and behaviour are being altered, without taking into account the threat to the value of authenticity, in all these regards, already caused by the disorder.

To be coherent, one must acknowledge that if comparable or even more severe alterations are caused by the TRD, this makes the patient less authentic, which, according to the logic of the criticized argument, is morally
problematic. Accordingly, a successful outcome of DBS could be viewed as a form of liberation since a hindrance for the patient to be authentic and live authentically is eliminated if the depression is vanquished or significantly reduced. Some examples could be improved health or quality of life, the ability to return to work, or establishing a relationship. If so, then the DBS treatment would be in accordance with, even promoting, the moral imperative of authenticity.

In addition to the main problem, we briefly address three other concerns also created by a superficial understanding of, and with more or less explicit references to, ideas of an authentic self. First, there is the idea that the depression is a part of, or at least perceived to be a part of, the patient’s personality or inner self. This view, coupled with a belief in the normative thesis of authenticity, can lead to the life-threatening conclusion that treating the depression is morally problematic, notwithstanding that the value of authenticity must be weighed against other moral values. Given the fundamental and disruptive changes caused by TRD, manifested in a person’s way of life before and during a depressive episode, it seems problematic to defend a belief that equates a severe disorder and an authentic self, and that treating the depression thereby is a threat to authenticity.

The next problematic argument suggests that the aim of an ethically acceptable DBS treatment, at least prima facie, should be to restore the person to a premorbid state. Though this suggestion might have an intuitive appeal, and does follow from a static view of the self, it does seem problematic at a closer look. Most of the patients with MDD considered for DBS have lived with the disorder for years or even decades. Considering the severe impact of the disorder, depression, as well as its treatment, is not likely to leave the patient unchanged. By way of example, we report of a patient with PD describing that she, after the DBS operation, experienced “a third version of me,” different from both the version of self-perception prior to PD and the version affected by the disease, but prior to the effective symptom relief provided by DBS. Similar accounts have been reported elsewhere in the literature. Given these reports, the suggestion that an ethically acceptable DBS treatment should restore a premorbid self seems both uninformed and unattainable, and is therefore not a suitable criterion for ethical DBS.

The final comment addresses an epistemic difficulty facing arguments based on the value of authenticity, to determine what version of the self is
the authentic self. Life changing experiences are not only caused by severe disorders, but by living and learning. Beliefs in an authentic self, given by nature and unchanged by time, are persistent, but are challenged by science. As we mention in an example, it cannot be ruled out that it is only through effective medication – or equally momentous changes – that some patients for the first time in their lives will report that they experience their true selves. So is it possible, and if so how, to determine which version of the self is authentic?

Given these examples, arguments based on the value of authenticity must be used with great caution. Nevertheless we suggest that the concept of authenticity could be employed to capture and analyse an intuition expressed both in ordinary life and by ethicists – that some alterations of cognition, mood and behaviour are ethically objectionable, whereas others are unproblematic or even desirable. The concept of authenticity can, if sufficiently specified, illuminate ethical concerns regarding changes of a patient’s fundamental defining characteristics including how these characteristics vary from patient to patient, and, over the lifespan of a single patient.

**Paper IV: Thinking Ahead on DBS**

The main problem addressed in paper IV is that the current debate on ethics and DBS has neglected important perspectives regarding upcoming and future DBS concerns. Present-day bioethical concerns can and do change. We argue that if this fact is overlooked, and only current DBS concerns raised by current DBS technology are addressed, the analysis may soon become dated. The future-oriented contributions thus far tend to fall into this trap, even though it addresses ethical implications of for instance new insertion techniques, improved patient selection, novel brain targets and new indications, as well as on ethical implications for DBS if other therapies were to improve and questions on human enhancement. These are very important perspectives, but equally important perspectives remain understudied. Thus, the main objective of the article is to discern how ongoing and continuous changes, both regarding technology and moral attitudes, impact an ethical analysis of DBS, i.e. to illuminate the
contextually shaped transience of bioethical concerns. However, although DBS technology is the main subject matter of this particular paper, note that we do not suggest that technology is the only key to foresight.

It is surprising that the ethical implications of new generations of DBS technology have not been addressed by ethicists and philosophers interested in brain stimulation, considering that some of this technology is already in the pipeline. We approach this question by introducing a distinction between inherent and noninherent ethical concerns (IECs and N-IECs, respectively). In short, the IECs arise from the defining features of the DBS technology per se, whereas the N-IECs are identified by a negative definition, referring to all bioethical concerns that are not IECs. Since the IECs are inseparable from the defining features of the technology, these ethical concerns can only be impacted by changing preferences. The N-IECs, on the other hand, can – among other things – originate in current technological shortcomings, in a technology that is yet to be optimized, and can therefore be impacted by technical advancement. Using features of the DBS technology as examples, we argue that many of the currently identified ethical problems with DBS, such as stimulation induced mania, are N-IECs. These challenges can be addressed by refining the DBS technology, while for instance problems created by an altered body image due to the mere fact of being implanted, thus an IEC, cannot. On the other hand, such concerns are only experienced by some users, and they can change with changing moral attitudes. For instance, the familiar is often perceived as less problematic than a practice that has only recently been introduced.

By employing the distinction between IECs and N-IECs, we identify and make explicit the particular limits and potentials for change within each kind of bioethical concern respectively, including how present and upcoming bioethical concerns regarding DBS emerge and become obsolete. For instance, to heed the temporal feature of emerging bioethical concern, we distinguish between current concerns, foreseeable future concerns and unforeseeable future concerns. Thus, some concerns will not emerge until the technology has become sophisticated enough for new uses to be realized, such as the foreseeable future concerns on DBS for enhancement purposes. In addition, concluding how best to handle an ethical concern requires knowledge of what kind of ethical concern one is facing. Thus, making these contextual dependencies explicit, besides identifying how current bioethical concerns can change, also creates the opportunity to be proactive and, when
feasible, call for technical solutions to some of the current ethical concerns raised by DBS. That is, there could be a moral imperative to commence specific alterations of the DBS technology, giving the engineer a prominent role in ethical problem solving.

Nevertheless, it is important to bear in mind that the distinction between IECs and N-IECs is an analytical one. We do not claim that drawing the line will be easy in all real-life cases. As we see it, the strength of this novel analytical tool lies not in an ability to classify every single ethical concern, but rather with its potential for novel insights regarding the transience of many of our ethical concerns. In addition, we show why current analytical tools, such as the distinction between ethical concerns raised by research and clinical practice respectively do not suffice to do justice to the complexity of changing ethical concerns. Still, every attempt to make a prognosis of what ethical challenges DBS will be facing ahead should be undertaken with trepidation. However, considering the rapid developments within neuroscience today, where DBS is just one example, this task must nevertheless be undertaken to avoid that the ethical analysis lags too far behind.

To conclude, this paper makes specific contributions to the debates on DBS, neuroethics and bioethics. The main novelties of the paper are to draw attention to, as well as widening the scope and understanding of, upcoming and future ethical concerns raised by DBS; to emphasize the contextual dependencies as well as the changeable nature of bioethical concerns, more specifically to close the lacuna regarding how some normative problems are dependent on technological states of affairs, as a new generation of DBS implants exemplifies; and to introduces the distinction between IECs and N-IECs as a novel analytical tool within bioethics. In addition, we also discuss and provide a new take on DBS and the questions of authenticity and enhancement.
THINKING AHEAD

We are always in the hands of our methods. Our current knowledge of the brain is determined by the methods by which it is examined; we see what we can measure, but the rest of the story is left untold. This holds true also in ethical analysis. Since I could not address the kind of questions I was interested in with the available methods, I had to develop analytical tools that could get the job done. I believe that the path of embedded ethics is worth pursuing, to see what conclusions it can obtain when applied to other topics than BMIs and DBS. The same goes for the distinction between IEC and N-IEC, introduced in paper IV. I find it likely that one of the reasons the relevance of a refined technology had not been addressed previously was the lack of an analytical tool for detecting such alterations. If this is a correct observation, we should consider what other important perspectives we may be missing due to the lack of an adequate analytical framework.

It is therefore worthwhile to identify fields of research that may benefit and bring new perspectives to an ethical analysis. For instance, when the subject matter of ethical consideration is as spectacular as BMIs, easily blurring the line between science and science fiction, the risk of both exaggerated hopes and fears is imminent. As exemplified most clearly in paper III, these and other biases increase the risk of fallacies in our ethical reasoning; for instance arguments based on unfounded assumptions and gut feelings instead of facts. At the same time, focusing on biases begs the question of where one’s own analysis may be flawed. The risk of arbitrariness behind the claims of what is – or is not – to be regarded as a
bias cannot be altogether neglected, and moral judgements are no exception to this rule, as research by for instance Joshua Knobe and successors have shown.\textsuperscript{171} I therefore believe that my future research would benefit from integrating research on biases as such.

Although this thesis targets some key ethical concerns raised by BMIs and DBS, there are in my opinion many issues that still need to be addressed. With regard to my aim to discern and elaborate on urgent or prominent concerns elicited by BMIs developed at the NRC, I have primarily addressed concerns elicited by stimulating, i.e. modulating, the brain, and to some extent the concerns raised by the use of nanotechnology. However, this focus leaves other concerns largely unattended, such as those elicited by substituting dysfunctional body parts and functions with technology, those elicited by neural control of external objects and those elicited by new discoveries regarding the brain and the mind. Additional concerns may arise due to novel Brain-to-Brain Interfaces, which will allow individual brains to share sensorimotor information in real-time. The first successful experiment on such an interface was published in early 2013. In short, tactile and motor information was recorded from cortical neurons in one rat and transmitted to the cortex of another rat. The researchers conducting the experiment suggest that this interface could, at least in theory, connect a number of brains, creating a multi-brain system; something that could possibly create the first “organic computer capable of solving heuristic problems”.\textsuperscript{172} The novelty and potential of BMIs has also been demonstrated by letting a monkey in the US, implanted with a BMI, manoeuvre a monkey avatar in Japan, by neural control alone. Moreover, cognitive neural prostheses are under development. Theodore Berger, at USC, is heading the research on a BMI to substitute parts of the hippocampus in the attempt to restore and enhance memory...

\textsuperscript{171} For instance, the work of Joshua Knobe have shown that people treat ‘harm’ and ‘help’ scenarios differently, the so-called Knobe effect; a bias that likely effect philosophers as well.

\textsuperscript{172} Pais-Vieira, et al., 2013
Thus, there are many applications of BMIs, both current and upcoming, which still call for ethical analysis. For instance, with these new possibilities maybe the question on personal identity must be revisited; or even our views on identity as such.

The frontiers of neuroscience are rapidly forging ahead; the ongoing development of BMIs is just one example. Still, we are at present far from unravelling the secrets of the brain. Thus we must remain humble before this knowledge gap, and expect continuous revisions of our current beliefs about this crème de la crème of organs. Even established scientific truths can change, a fact exemplified by disproving the old dogma that there is no neurogenesis in adult brains. BMIs give us the opportunity to explore and impact the brain from within, and may enable major breakthroughs within neuroscience, especially as the technology gets more refined. This in turn calls for both conceptual and ethical analysis. Some neuroscientists already challenge beliefs that are cornerstones in our way of life, for instance by claiming that notions such as the self, agency and the ability to make choices are explanatory fiction. What shall we make of such claims? Some of these claims have been disputed by referring to “the extrapolation of results from highly simplified laboratory situations”\(^{174}\), but one can also understand such claims as yet another reason for engaging researchers from the humanities and related disciplines in neuroscience of the 21st Century. For instance, is it even possible to reduce complex phenomena such as free will and consciousness to firing neurons alone? I do not question that there is a neural basis for these phenomena, but we must distinguish between different analytical levels if we are to properly address these issues. As suggested by the renowned cognitive neuroscientist Michael Gazzaniga: brains are not free, but people are. We cannot extrapolate from the micro level (deterministic neurons) to the macro level, which involves behaviour and social interaction between people. By pointing to phenomena such as

\(^{173}\) Li, et al., 2012

\(^{174}\) Nuffield Council on Bioethics, 2013, p 75
emergence and downward causation, i.e. how the mind constrains the brain, Gazzaniga suggests that we are sufficiently free to be held accountable for our actions.\textsuperscript{175}

I recently encountered the phrase “neuro is the new nano”. While concluding this thesis in late 2013, there seems to be ample support for this claim. This year alone two impressive brain initiatives have been launched: The NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative\textsuperscript{176} and the EU Human Brain Project (HBP).\textsuperscript{177} Both projects will incorporate and address ethical concerns, and are characterized by a truly interdisciplinary environment. Though the size of these projects differs from most research consortiums, they can still be viewed as a sign that the traditional way of conducting and organizing brain research is transforming – and for good reasons. Considering the prominent status of the brain and the potential benefits enabled by BMIs, it would be unfortunate if the ethical analysis of these very developments lag behind. The need for ethical analysis is accentuated when considering the market shares at stake for each new application of a functional BMI. As shown by for instance the impact of the frequent advertising on psychopharmacological drugs in the US, market forces need to be balanced and new neurotechnologies must be examined critically, yet still heed both the possibilities and limitations of BMIs. By encouraging and facilitating the inclusion of embedded ethicists in research projects, an ethics analysis can be proactive and influence the development of research protocols as they are initiated and implemented. The embedded ethicists can have a direct impact on the research while it is being conducted, and thereby challenge the idea of technological determinism. Conversely, the scientists can have an equally important impact on the ethical analysis by safeguarding that the embedded ethicist’s understanding of the subject matter under ethical analysis is correct and by

\textsuperscript{175} Gazzaniga, 2009
\textsuperscript{176} NIH, 2013
\textsuperscript{177} EU, 2013
adding important scientific perspectives that the ethicist may not catch or where important subtleties may go unnoticed.

However, I do not believe that we should halt there. Another insight obtained during my research on DBS is the need for patient participation and interactions. During my years at the NRC, I have attended a number of conferences and workshop, and I find it quite striking that only one included DBS patients as invited speakers and participants. The call for scientifically informed ethicists has come from empirical ethics as well, but to my mind, patient integration is of equal importance. First, patients’ and research subjects’ experiences are essential both for a medical and ethical evaluation of DBS. This therapy is not curative; DBS facilitates symptom control with the aim of improving quality of life for the users. The few published reports that focus on first person perspectives on living with DBS, support the need for this inclusion. Publications entitled ‘Neurosurgery in Parkinson’s disease: the doctor is happy, the patient less so?’\textsuperscript{178} and ‘Neurosurgery in Parkinson disease: a distressed mind in a repaired body?’\textsuperscript{179} tell us that a medical evaluation of the outcome of DBS is not sufficient to safeguard that quality of life will improve after the procedure. More research is warranted to determine whether these are anecdotal findings or if they bespeak a recurring phenomenon. It is equally important to determine what the key concerns may be, and if there are ways to address them and achieve a better overall outcome in terms of patient satisfaction.

Besides calling for research mapping and evaluating these experiences, I also call for a stronger integration of patients and research subjects into the research process itself – for embedded BMI users alongside embedded ethicists and other researchers. Just recall the upcoming BMI devices that indisputably breach the realm of science fiction. It is not unreasonable to expect that our present moral intuitions will not suffice to address and

\textsuperscript{178} Agid, et al., 2006
\textsuperscript{179} Schüpbach, et al., 2006
elaborate on these new experiences. Here close interaction with the actual users seems essential to avoid arguments based on moral ‘common sense’, which in these extreme and novel situations may turn out to make little sense at all. As I argued in paper IV, moral attitudes change over time and with new experiences. Conversely, both clinicians, BMI developers, ethicists and other involved parties risk building their analysis on their own unfounded assumptions (equally as problematic as the above mentioned examples) on what matters from a user-perspective.

Even if only a few of the promises entailed in this next generation of BMIs are fulfilled, the societal impact may be considerable. Therefore it seems problematic to leave the discussions, and decisions, to the experts alone, be they scientists, clinicians, ethicists or other researchers. These questions concern everyone, and wherefore decisions regarding our future must, according to my point of view, be transparent, and engage and involve the public as well as researchers and other key stakeholders. To paraphrase the title of a book by British philosopher Jonathan Glover – What sort of people should there be, and what sort of future world do we want? Ethicists and other researchers from the humanities and social sciences can help in discerning and elaborating important perspectives, which was my intention with this thesis. Do we want Humanity 2.0? Are our reasons for affirming or rejecting this idea sound, or based on unfounded assumptions, biases and a general unfamiliarity with the scenarios we are deliberating? I do not have the answers, but it seems essential that these questions are raised both within academia and in society at large. What I do believe though, is that there is too much potential in these techniques to not take the ethical and scientific challenges of BMIs seriously.

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180 Glover, 1984
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