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Deflating the “DBS causes personality changes” bubble

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Abstract The idea that deep brain stimulation (DBS) induces changes to personality, identity, agency, authenticity, autonomy and self (PIAAAS) is so deeply entrenched within neuroethics discourses that it has become an unchallenged narrative. In this article, we critically assess evidence about putative effects of DBS on PIAAAS. We conducted a literature review of more than 1535 articles to investigate the prevalence of scientific evidence regarding these potential DBS-induced changes. While we observed an increase in the number of publications in theoretical neuroethics that mention putative DBS-induced changes to patients’ postoperative PIAAAS, we found a critical lack of primary empirical studies corroborating these claims. Our findings strongly suggest that the theoretical neuroethics debate on putative effects of DBS relies on very limited empirical evidence and is, instead, reliant on unsubstantiated speculative assumptions probably *in lieu* of robust evidence. As such, this may reflect the likelihood of a speculative neuroethics bubble that may need to be deflated. Nevertheless, despite

the low number of first-hand primary studies and large number of marginal and single case reports, potential postoperative DBS changes experienced by patients remain a critical ethical concern. We recommend further empirical research in order to enhance theoretical neuroethics work in the area. In particular, we call for the development of better instruments capable of capturing potential postoperative variations of PIAAAS.

Keywords Adverse effects · Autonomy · Agency · Assumption · Authenticity · Control group · Deep brain stimulation · Evidence · Identity · Neuroethics · Personality · Self

Introduction

In theoretical neuroethics, the idea that “personality changes and possible loss of personal identity can follow from the introduction of foreign (biological or technical) material into the brain” [1] is pervasive and highly recurrent. In particular, deep brain stimulation (DBS) has been commonly associated with such alleged changes, and consequently, it has been a central concern in theoretical neuroethics. Many publications suggest that when “DBS is applied to enhancing or maintaining movement, the specter of Phineas Gage, whose personality changed so radically after his brain was pierced by a tamping iron, haunts us. [DBS] may fundamentally alter selves” [2].

Suggestions that DBS may induce personality changes are strongly established within theoretical neuroethics narratives, and they are articulated in many ways. For instance, Schechtman declares that “personality changes [following DBS] represent a threat to personal identity

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and agency” [3]. Witt and colleagues assert that “the risk of becoming another person following [DBS] surgery is alarming” [4]. Others argue that DBS “pose[s] manifold medical, philosophical and ethical questions as regards the personality, personal identity, individual responsibility, autonomy, authenticity and self-perception of the person involved” [5]; or that DBS “may alter a range of mental states critical to thought, personality and behaviour ... disrupt[ing] the integrity and continuity of the psychological properties that constitute the self and one’s experience of persisting through time as the same person” [6]; or that DBS “has the potential to alter essential features of a patient’s personhood, including mood, personality, and cognitive abilities” [7], etc. These examples are a fraction of many claims frequently published in neuroethics articles about the alleged adverse effects of DBS. In fact, since the publication of Schüpbach et al.’s seminal work in [8], entitled “Neurosurgery in Parkinson’s disease: A distressed mind in a repaired body?” [8], there has been a substantial increase in theoretical neuroethics articles exploring the putative impacts of DBS on personality, identity, agency, autonomy, authenticity, and self (PIAAAS). The idea that DBS induces PIAAAS changes is so deeply entrenched within neuroethics discourses that it has become an unchallenged narrative. However, it comes with some surprise that this narrative has not been rigorously scrutinized. To our knowledge, few studies investigate the occurrence and type of empirical evidence demonstrating putative effects of DBS on PIAAAS.

The purpose of this study is to address this issue. We critically examine and assess empirical evidence about the putative effects of DBS on patients’ PIAAAS. In particular, our main objective is to identify evidence within the neuroscientific and medical literature substantiating the conclusion that DBS causes PIAAAS changes, which appears to be persistently suggested in the theoretical neuroethics narrative. Accordingly, this paper targets substantial and consequential effects impacting patients’ PIAAAS, primarily considering deteriorative and estrangement-inducing adverse effects of DBS [9]. Our second objective is to examine the prevalence of articles discussing the alleged effects of DBS on patients’ PIAAAS in the theoretical neuroethics literature. Our third goal is to assess our findings, especially, whether the theoretical neuroethics literature is engaged in a speculative bubble, which may need to be deflated and rectified by grounding it in empirical evidence

as available through the scholarly neuroscientific and medical literature.

Methods

To identify and examine the prevalence of articles discussing putative effects of DBS on patients’ personality, identity, agency, authenticity, autonomy, and self (PIAAAS), we searched the archives of some leading 30 bioethics journals¹ and AJOB Neuroscience, as well as relevant articles indexed in ProjectMUSE, JSTOR, PhilPapers, and PhilIndex (limiting our search to academic journals). Furthermore, we examined the prevalence of empirical evidence supporting links between DBS and PIAAAS explicitly. To this purpose, we searched for relevant articles in the databases of PubMed, Scopus, Embase, Web of Science, PsycArticles, Psychology & Behavioral Sciences Collection (PBSC), PsycInfo (via Ovid), and Psychiatry Online (excluding news articles). Articles until May 2017 were considered.

Articles were retrieved using the search terms “*deep brain stimulation*” AND (*personality OR identity OR autonomy OR agency OR authenticity OR self*). Duplicate articles were removed manually with the help of EndNote’s “Find duplicates” function. To determine whether articles were mainly discussing DBS, we used the web browser’s (Google Chrome) or Adobe Reader’s search function to get an overview of the extent to which the term DBS appeared in each article under review. Articles that did not mention DBS in the abstract or did not dedicate at least half of the text to discussing DBS were excluded. The remaining articles—those that involved ‘substantial’ discussion of DBS—were then individually examined to determine the number of times any element of PIAAAS was mentioned as determined through a search for (*personality OR identity OR autonomy OR agency OR authenticity OR self*) using the browser or Adobe Reader’s Search function. The number of mentions for each search component were then tabulated in an Excel sheet. Articles that did not mention at all any component of PIAAAS were automatically excluded. The abstract and/or actual text of articles that mentioned any of these terms were examined further to see if they really explored the effect of DBS on PIAAAS or if these terms were just mentioned in passing. In some

¹ Please refer to Annex 1 to see the full list of journals.

cases, bioethics articles might make over 100 mentions of the terms PIAAAS (taken collectively), while scientific articles might make as little as five (or fewer) of the same mentions (taken collectively).

Articles reporting primary studies or case studies were identified and examined manually. We defined primary studies as new reports of clinical cases involving first-hand interviews or clinical studies involving implanted patients. In other words, a first-hand primary study is a new clinical report involving at least one patient undergoing psychometric tests or being consulted in a clinical setting or being interviewed for the purpose of examining potential DBS-induced PIAAAS. Our final inclusion and exclusion criteria were based on the evaluation of the primary study’s core text and explicit conclusion. Articles with primary data were identified as first-hand literature; consequently, articles that did not directly gather PIAAAS-relevant data from patients were not considered as valid first-hand evidence. Articles not reporting novel empirical evidence but that still discuss already published primary empirical studies in relation to PIAAAS were manually identified as second-hand literature. Articles that discuss PIAAAS but not referring to any primary research (of a kind that reported new empirical evidence) were manually identified as third-hand literature.

Results

In General

A total of 1535 articles were assessed. We found 64 articles that qualified as first-hand studies (See Fig. 1 “Primary Study Articles”²). However, after assessing these articles one by one, we found that 67% ($n = 43$) do not support direct links of DBS on PIAAAS. Analysis of the remaining 21 articles revealed that 13 articles were marginal or single case studies.³ As a result, only 8 studies qualified as significant evidence (12.5% of 64

primary research), involving 168 patients in total (see Table 1: First Hand Primary Research).⁴ It is crucial to note that none of these 8 studies had control groups. Generally, it can be more difficult to evaluate the outcome and attribute the cause of the observed effect when a control group is lacking. Prospective, randomized, and sham-controlled trials, for example, represent particularly neat study designs to investigate effects of DBS. Strikingly, when a control group was included as part of the experimental procedure, for example in Schüpbach et al. [18], the control group, which did not receive stimulation, experienced more severe adverse effects related to PIAAAS than the actual group that received stimulation.

We observed a contrast between the number of publications in theoretical neuroethics and the number of published primary research articles (see Fig. 2). A substantial increase in publication in theoretical neuroethics appears to occur starting in 2009.

In Particular

1) Conclusions of studies not matching neuroethics claims

When assessing the strength of evidence referred to in the theoretical neuroethics literature, we observed that the most cited articles in Table 1⁵ are three seminal manuscripts published by Schüpbach et al. [8], Agid et al. [11] and Houeto et al. [10]. Interestingly, the articles by Schüpbach et al. [8] and Agid et al. [11] are two distinct versions of the same French trial study, based on the same interviews, involving the same 29

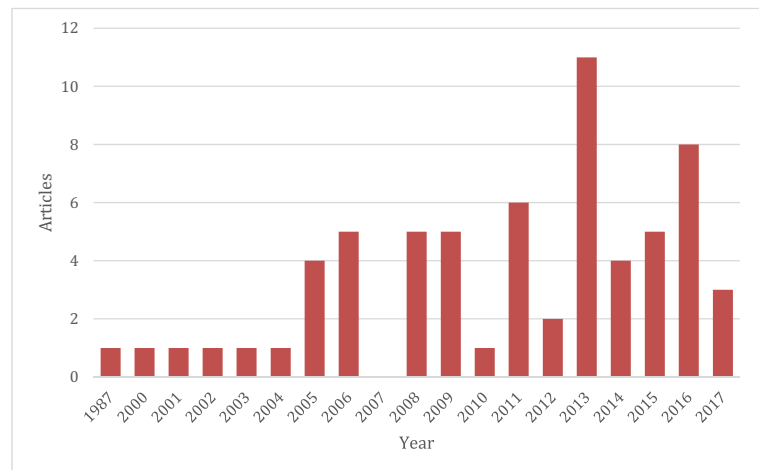
² Primary study articles explicitly naming PIAAAS in their published work.

³ By marginal reports, we understand case reports not well detailed. Marginal reports mention some events in articles, nothing more. For instance, most articles marginally report “out of 27 patients implanted, 1 patient experienced hyper-sexuality following surgery” without providing more details. From marginal reports, it is difficult to derive causation, in particular also impossible to exclude co-variables. Hence, by marginal reports we include anecdotal reports, single-patient case reports.

⁴ Involving 168 patients in total, but not all 168 patients’ experiences would qualify as evidence for a link between DBS and PIAAAS changes. Even if marginal and case reports were included in our final total, it would not significantly change the prevalence (see our Discussion). To our knowledge, the most cited case report in neuroethics is the one by Leentjens et al. [17]. Unfortunately, most marginal and case reports in the literature are not like Leentjens et al. [17]. The report of Leentjens et al. is a unique example where clinicians were turning off/on the stimulation and were able to directly and instantaneously observe behavioral changes occurring (accordingly, they were capable of excluding some variables as contributing to these changes). But if we include the Leentjens et al.’s single case report in our final count, we have to include all the marginal case reports. Most marginal reports strictly mention events in articles, without providing much details or excluding co-variables. Including marginal case reports would be including occurrences where essential details about the cause of the observed changes are missing.

⁵ As reported by Google Scholar citation metrics

Fig. 1 Number of primary articles on the putative effects of DBS on patient PIAAAS until May 2017



patients. Despite being referenced, cited, and discussed in theoretical neuroethics as empirical evidence demonstrating the effects of DBS on PIAAAS, both articles do not support this conclusion. Agid et al. [11] concluded:

It seems more likely that the difficulty in social integration experienced by our operated patients resulted, not directly from a modification of the patients' personality, but rather indirectly from a difficulty of reintegrating into the socio-familial and professional environment [11].

At the same time, Schüpbach et al. [8] concluded:

it was shown that [DBS] led to an overall improvement in mood, anxiety, and quality of life. Now, in spite of the excellent motor outcome, it is clear that the operation can result in poor adjustment of the patient to his or her personal, family, and socio-professional life. Whether this is a purely reactive response to a new situation or whether it is caused by an effect of STN stimulation on behavior, or both, remains to be elucidated. [8]

An article published later by Schüpbach et al. [18] that included a group of people with Parkinson's disease (PD) treated with DBS and a matched control group not treated with DBS (both groups with a follow-up period of 2 years), found that the control group experienced a higher rate of psychiatric adverse effects related to PIAAAS compared to the group treated with DBS.

On their side, Houeto et al. [10] reported 8 patients (out of 24) who experienced changes related to PIAAAS

following DBS implantation, but they observed that postoperative "psychiatric disorders consisted of amplification or decompensation of previously existing disorders that had sometimes passed unnoticed" before implantation [10]. In other words, DBS did not initiate the onset of postoperative psychiatric disorders; rather, patients were already suffering from these disorders prior to implantation. Put simply, Parkinson's disease symptoms may have 'masked' psychiatric symptoms; DBS helped keep Parkinson's disease symptoms under control, with the decompensation and manifestation of psychiatric symptoms as an unintended adverse effect.

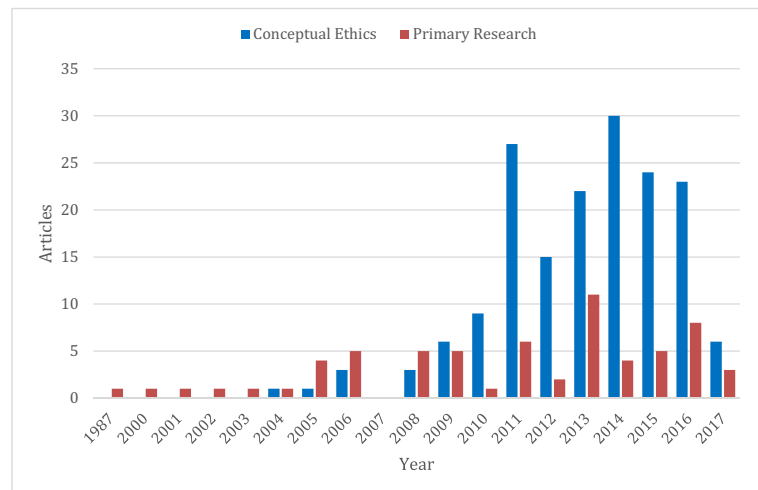
2) Conceptual discussions based on few quotes.

Given the scarce evidence, as reported above, many neuroethicists and philosophers selected specific quotes from "Schüpbach et al. [8]" or "Agid et al. [11]" to introduce, support, and illustrate their philosophical approach regarding the link of DBS to changes of implanted patients' PIAAAS. One of the most fascinating quotes used by conceptual neuroethicists is the reported experience of an implanted female French patient who declared after surgery: "I feel like an electric doll" [8]. Surprisingly, we found that this specific quote was not accurately translated in Agid et al. [11], where the patients' statement appeared as: "I'm an electric doll" [11]. We would like to highlight the importance of these semantic points because establishing a philosophical theory on a few selective quotes, particularly when words such as "I feel" or "I am" largely differ in their meaning, does not represent robust evidence.

Table 1 First hand primary research

Author(s)	Type of Patients	Title	Numbers of patients	Conclusion
Houeto et al. [10]	PD	Behavioural disorders, Parkinson's disease and subthalamic stimulation	24	8 out 24 patients displayed postoperative changes: however, the authors advanced that postoperative “psychiatric disorders consisted of amplification or decompensation of previously existing disorders”. In other terms, PD symptoms were inhibiting psychiatric disorders, but with stimulation keeping symptoms under control, some pre-existing psychiatric disorders were manifested.
Agid et al. [11]	PD	Neurosurgery in Parkinson's disease: the doctor is happy, the patient less so?	29	“It seems more likely that the difficulty in social integration experienced by our operated patients resulted, not directly from a modification of the patients' personality, but rather indirectly from a difficulty of reintegrating into the socio-familial and professional environment”
Schüpbach et al. [8]	PD	Neurosurgery in Parkinson disease: A distressed mind in a repaired body?	29 (same patients as Agid et al. [11])*	“It was shown that neurosurgery led to an overall improvement in mood, anxiety, and quality of life. Now, in spite of the excellent motor outcome, it is clear that the operation can result in poor <i>adjustment</i> of the patient to his or her personal, family, and socio-professional life. Whether this is a purely reactive response to a new situation or whether it is caused by an effect of STN stimulation on behavior, or both, remains to be elucidated.”
Gisquet [12]	PD	Cerebral implants and Parkinson's disease: a unique form of biographical disruption?	30	“DBS suppresses the most striking symptoms of Parkinson's disease, but at the same time the patient loses control over managing the illness and experiences significant changes in personality. Cerebral implants are a unique form of biographical disruption of which neither physicians nor patients measure the impact.”
de Haan et al. [13]	OCD	The phenomenology of Deep Brain Stimulation-induced changes in Obsessive-Compulsive Disorder patients: An enactive affordance-based model	14	No direct conclusion in relation to PIAAAS.
de Haan et al. [14]	OCD	Effects of Deep Brain Stimulation on the lived experience of Obsessive-Compulsive Disorder patients	18 (14 are the same patients from de Haan 2013).	“Apart from the previously documented improvement of mood, diminishment of anxiety, and increase of impulsivity, we also found changes such as an increase in trust, self-reliance, and self-confidence, a more unreflective mode of engagement, and a more careless stance on things.”
Lewis et al. [15]	PD	Subjectively perceived personality and mood changes associated with subthalamic stimulation in patients with Parkinson's disease	27	“Personality changes were perceived by six of 27 (22%) patients and by 10 of 23 caregivers (44%). [...] Our results show that a high proportion of PD patients and caregivers perceived personality changes under STN-DBS, emphasizing the relevance of this topic. Mood changed in positive and negative directions. Standard measurement scales failed to adequately reflect personality or mood changes subjectively perceived by patients.”
Pham et al. [16]	PD	Personality Changes after Deep Brain Stimulation in Parkinson's Disease	40	“STN-DBS in PD patients is associated with personality changes in the direction of increased impulsivity”. Impulsivity changes were mostly perceived by relatives not patients after 3 months of stimulation.

Fig. 2 Theoretical neuroethics and primary research articles on the putative effects of DBS on patients' PIAAAS until May 2017



This highlights the importance of not just basing theoretical arguments on some selective quotes. In addition, one would think that such nuances do make a difference in the theoretical discourse, even though, the error for disseminating a wrong translation was not on the part of neuroethicists, in this case. However, such a discrepancy in translation suggests that we (neuroethicists) should look more carefully from where these quotes are taken from and how they are being used (purportedly) as evidence within our work. Ontologically speaking, one could strongly question and dispute a philosophical conclusion based on the sentence “I feel like an electric doll”, as it might not entail the same philosophical view as the quote, “I’m an electric doll” (while the latter quote may involve a psychotic (delusional) episode, the former could simply represent a playful and moody remark). Importantly, this also means that professional interviewers have a duty to try identifying what the interviewees mean when verbalizing such statements, and more importantly, translations should be identical across different publications and should faithfully capture the verbal expressions voiced by patients, along with providing a description of the context in which these expressions were made. As well, this highlights that philosophers quoting these first-hand studies may need to provide more than just fragments of the quote, preferably include a longer tract of quoted text that better reveals the patients’ intended meaning, and mention the context as well, especially if this was reported or described in the primary study.

3) Postoperative outcomes related to pathology rather than technology

As indicated in Houeto et al.’s conclusion [10], a neurodegenerative disease such as Parkinson’s disease may entail psychiatric symptoms due to advancement of the degenerative process, a phenomenon that does not necessarily translate to other diseases, such as dystonia. Based on (still scarce) qualitative research outcomes, it could be suggested that postoperative adverse effects on PIAAAS are more related to disease progression rather than to DBS itself. For instance, interviews conducted by Hariz et al. [19], capturing subjective experiences of 30 patients implanted with DBS for treating their dystonia, reveal that, overall, patients felt they “still [were] the same person inside, but with new abilities and another physical appearance, [which] was difficult to comprehend and come to terms with”.¹² As an example, Hariz et al. [19] quoted a patient reporting: “Now, even though I have been given a new body I haven’t been given a new mind. It’s like plastic surgery, you might change your nose but how you feel about yourself is still the same” [19]. Elsewhere, de Haan et al. [14], after interviewing 18 OCD patients implanted with DBS, concluded that: “Apart from the previously documented improvement of mood, diminishment of anxiety, and increase of impulsivity, we also found changes such as an increase in trust, self-reliance, and self-confidence, a more unreflective mode of engagement, and a more careless stance on things” [14]. Our review found that when the putative effects of DBS on

PIAAAS are raised by theoretical neuroethicists, most authors do not distinguish diseases and stimulation parameters—most generalize their conclusions concerning the putative effects of DBS on PIAAAS of patients being treated for Parkinson’s disease to how they understand the effects of DBS on PIAAAS for patients with other conditions and potentially, with leads implanted in other brain regions or with different stimulation parameters. The presumption here is that all patients suffering from different presenting neurological conditions and stimulated in different brain regions and with differing parameters would react in the exact same way to treatment. For example, Nyholm and O’Neill [20] in their conceptual study about the effects of DBS on treatment-refractory anorexia nervosa individuals selected cases from different patients implanted with DBS targeting distinct pathologies: for instance, Parkinson’s and OCD. Our findings show that there is no evidence pointing toward an identical treatment reaction for DBS targeting different neurological conditions. Although we do not say that unintended effects of DBS can be excluded *per se*, we aim to highlight that theoretical neuroethics publications should always acknowledge that DBS is not a monolithic technology and that the region and parameters of stimulation interact with the pathophysiology of the disorder, all of which contribute to the overall effect of the surgery and stimulation.

4) Assumptions

We discovered some commonly accepted assumptions among conceptual neuroethicists and philosophers, particularly in third-hand literature. Assumptions include claims without any corroborating empirical evidence. In those cases, manuscripts discuss putative impacts of DBS on PIAAAS without referring to first-hand primary research. For instance, in order to support the hypothesis that implantable devices are a philosophical and ethical problem, Schermer [21] quotes Hasson’s view that brain implants may be a “reason to reconsider our criteria for personal identity and personality changes” [1]. It is essential to note that Hasson’s conceptual paper does not refer at all to any first-hand primary research. Elsewhere, Johansson et al. advance the claim that, “[p]otential alterations of personality seem [...] to be relevant for most DBS indications” [22]. It is important to

note that these same authors, in other important works, refer to first-hand primary research [23, 24]. However, these examples of unsubstantiated claims—i.e. claims lacking any reference to primary research—as appearing in third-hand literature illustrate a trend across the theoretical neuroethics literature where authors rely on rare empirical evidence to argue their case, as statements based on lack of evidence go unchallenged. It goes without saying that purely theoretic work is warranted and highly valuable. Neuroethicists have more than the freedom to reflect on PIAAAS, but it is potentially misleading if they either bring it in connection with empirical findings that do not corroborate their claims.

To the best of our knowledge, the assumption that DBS alters PIAAAS first appears to have been explicitly articulated in a scholarly publication with the work of Gisquet [12]. Gisquet, interviewing patients implanted with DBS, declared that her study was “based on the assumption that a treatment using biotechnical techniques is a unique disruptive experience which redefines the patient’s life” [12]. Incidentally, from the moment the assumption was formulated and published in the literature in 2009 (see Fig. 2), across all publications in neuroethics, the prevalence of theoretical manuscripts increased, while studies reporting empirical evidence diminished overall. Although speculation in ethics can be a very valuable tool [25], the lack of empirical evidence showing that DBS induces PIAAAS changes is concerning and reflects a potential speculative ethics bubble, which might need to be deflated.

Discussion

In general, we found that the discussion about putative effects of DBS on patients’ PIAAAS in theoretical debates is supported by only a small sample of empirical evidence, which strongly suggests that this discussion relies on a limited amount of facts rather than on substantial empirical evidence. Theoretical neuroethics in the context of DBS-related discussions about PIAAAS is mostly reliant upon second-hand and third-hand literature.

There is considerable diversity in the way putative effects of DBS on patients' postoperative life have been described in the literature, particularly in theoretical neuroethics (see Table 2: Sample of philosophical explanations about putative impact of DBS on PIAAAS). These descriptions seem to serve the authors' philosophical accounts rather than reflect first-hand primary study conclusions. For instance, according to Kraemer [33], "by employing the philosophical framework of authenticity and alienation, we are led to call into question the psychological assessment of the three case studies of Parkinson patients who underwent changes in their personalities and preferences after successful treatment with DBS". To support her claims, she refers to Schüpbach et al. [8]. However, as indicated above, Schüpbach et al. [8] do not conclude that patients' personalities were impacted by DBS.⁶ Elsewhere, Witt et al. [4] assert "we will begin our discussion with a few quotes from a case reported by Schüpbach et al. It will give us an impression of what proponents of the Change-of-Identify Thesis presumably have in mind when ascertaining 'alterations in the patient's identity'. Here too, there seems to be a misinterpretation of the findings of Schüpbach et al., who do not conclude anything about how DBS impacts patient identity."⁷ In a very influential paper (citation count 90 with Google Scholar at the time of writing), Baylis affirms:

"DBS is such a threat but only insofar as it is a threat to agency—the ability to make informed and rational choices—as when a person's actions do not flow from her intentions or beliefs but rather are the result of direct brain manipulation. Here it is worth noting that following DBS patients not only report "I don't feel like myself anymore," and "I haven't found myself again after the operation," they also report "I feel like a robot," and "I feel like an electric doll".

To support this philosophical claim, she refers to Schüpbach et al. [8]. However, Schüpbach et al.'s [8] article explicitly states that these quotes: "I feel like a robot," and "I feel like an electric doll" are given in the context of discussions of "altered body image", not agency. For instance, Schüpbach et al.'s [8] manuscript

states: "1) Altered body image: Only 6 patients (20%) thought about the implanted material in terms of body image and formed a mental representation of the stimulator and the electrodes." Schüpbach et al.'s [8] do not suggest anything about how DBS might alter patients' deliberation, decision-making or agency. Our goal here is not to single out each relevant claim made in the philosophical and theoretical neuroethics literature and to check whether it is supported by empirical evidence. After all, part of the important mission of philosophy and theoretical neuroethics, as seen in the great conceptual work of Baylis and others cited above, is to speculate about concepts and to indulge in thoughtful enquiry, not necessarily trying to ground them in empirical facts. Instead, our goal is to stress that Table 2 represents a sample of some of the philosophical speculations about the putative impacts of DBS on PIAAAS, which appear not to accurately reflect the conclusions made by the first-hand primary studies.

Out of 64 first-hand primary studies, 43 did not corroborate evidence that DBS leads to PIAAAS alteration. Out of the remaining 21 articles, 13 were marginal or single reports. By virtue of the fact that marginal or single observations do not constitute robust data leading to definitive scientific conclusions, our study indicates that the theoretical neuroethics literature may rely on unsubstantiated speculative assumptions *in lieu* of robust evidence. Marginal or single findings are discounted because they are mostly reported without any objective measurement and may not include extensive medical information, which make these studies difficult to replicate and compare with other studies. In addition, they do not provide the actual incidence of DBS-induced PIAAAS in a particular cohort of individuals that received DBS for a particular disorder in that institution. In general, to establish cause-and-effect relationships, study subjects, for example, can be divided into experimental and control groups. Therefore, double blind randomized controlled trials (RCT's) are considered one form of study design (besides e.g. longitudinal and time series studies) for establishing such relationships [40]. In RCT's, differences in outcomes are attributable to different treatments received in such between-group designs because the distribution of confounders is balanced across experimental conditions by design [41]. In comparison to control-group designs, case-studies are often characterized by poor internal validity due to the fact that there is nothing to compare the result to. As a final addition, in principle, studies and reviews investigating

⁶ Not only Schüpbach et al. do not conclude this, they exclude personalities as an explanation in their Agid et al. [11] version. See our section "Conclusions of studies not matching neuroethics claims".

⁷ In addition, the concept of identity is not alluded to nor is used once in this published study.

Table 2 Sample of philosophical explanation about DBS putative impact on PIAAAS

Discussed by	DBS impacts characterised by
Gisquet [12]	Changes in personality and loss of control over one’s life and illness
Synofzik & Schlaepfer [26]	The ‘level’ and ‘extent’ of changes to naturalistic notion of personality
Focquaert & De Ridder [27]	Changes in personality and self-perception
Glannon [6]	Changes in thought and personality
Schechtman [3]	Narrative identity and agency/disruption of the narrative flow
Klaming and Haselager [28]	Disruptions of psychological continuity impact on patient competence and responsibility
Johansson et al. [22]	Personality changes and impacts on authenticity
Schermer [23]	Balancing risks and benefits and respect for autonomy and responsibility
Baylis [29]	Disruption of the balance between how a person sees and understands herself with how others see and understand her
Nir & Walter [30]	Personal identity and a sense of free agency (identification)
De Haan et al. [13]	Patients experience a richer field of affordances and act more flexible on these new affordances
Witt et al. [4]	Patients’ core attitudes
Gilbert [31, 32]	Self-estrangement, loss of control and powerlessness.
Kraemer [33]	Felt-Authenticity and felt-Alienation
Mecacci & Haselager [34]	Psychological maladaptations and conceptual schemes concerning the relationship between mind and brain
Dings & de Bruin [35]	Aspects of the self – embodied, experiential, affective, intersubjective, psychological/cognitive, narrative, extended and situated
Maslen, Pugh & Savulescu [36]	DBS can potentially affect authenticity of the patient’s choice.
Mackenzie & Walker [37]	Autonomy, competence
Nyholm & O’Neill [38]	DBS can bring about a patient’s “true self”: best version or the best part(s) of a person as valued from the point of view of the patient or from the point of view of a third party (e.g. the family).
Goddard [39]	The impacts of DBS must pay account to the interrelation of identity or agency or autonomy

effects on PIAAAS should differentiate between active and inactive control groups because there is a difference in the kind of effect estimates that are obtained [42].⁸ It is

⁸ This observation does not mean that for establishing causal relationships, there has to be a control group installed; having control groups is one example of good experimental design in order to compare effects. However, with regard to interventional DBS studies on cognitive changes, a recent review outlined that the majority of such studies is actually under-powered thereby affecting the inferences that can be drawn from such results (i.e. studies lacked statistical power even for large effect sizes and therefore are associated with an increased type II error risk [43]) Effect size refers to a standardized measure that quantifies the size of the difference between two groups or the strength of association between two variables (i.e. the magnitude of the effect). It goes without saying that studies on the presumed effects of DBS on PIAAAS should also be adequately powered. We are aware of the fact that recruiting age-, medication- and disease-matched controls and adherence to robust study designs are often practically difficult. A more detailed discussion on study designs (including, for example, interventional pre-post analyses), however, is beyond the scope of this article

essential to stress that these observations do not lead to the conclusion that case study designs are less valuable than RCTs in all respects.

According to a Global Deep Brain Stimulation Devices Industry report, in 2018, 21 companies are commercialising DBS worldwide⁹; Medtronic accounts for 150,000 implanted patients alone [44]. As such, accounting for the exact number of patients implanted with all different commercialized DBS devices worldwide is difficult to guess, but 150,000 is clearly an underestimation. Given the high number of patients

⁹ These companies include Boston Scientific Corp., Abbott Laboratories, Aleva Neurotherapeutics SA, Deep Brain Innovations LLC, Beijing Pins Medical Co. Ltd., etc. They are commercialising and manufacturing their devices across US, Canada, Japan, Europe, Asia-Pacific, Latin America. Please refer to <https://www.prnewswire.com/news-releases/global-deep-brain-stimulation-devices-industry-300594349.html> Last retrieved May 06 2018.

implanted with DBS, the number of reported (putative) DBS-induced PIAAAS changes appear to be extremely low. Cumulatively, our study found that there were only 168 patients interviewed across the 8 first-hand primary studies. Even if we were to include the 13 marginal and case reports we found, it would not significantly change the prevalence of evidence.¹⁰

The putative effects of DBS on patients' PIAAAS has probably been inflated in several ways. First, there is the problem of scarce data given that a large proportion of the published studies involve reports of only marginal or singular cases, and it is not possible to derive conclusions from this basis for explaining the phenomenology of DBS. For instance, a scholar who has read reports of marginal findings that some patients experience mood changes following DBS implantation might extrapolate that these mood changes are evidence of postoperative PIAAAS changes, even though mood changes are not sufficient to the ascription of DBS induced changes on PIAAAS. Deriving conclusions from marginal cases might lead to committing a *post hoc ergo propter hoc*-related error [9]. The phenomenon of “becoming a different person” after DBS interventions could not be solely attributed to the electrical stimulation itself but also to post-operative treatment adjustments or to disease progression [47, 48]. As such, the prevalence and incidence of effects on PIAAAS might not be exclusively correlated with a specific DBS target and/or stimulation parameter. It should rather be seen as a result of the interaction between electrical stimulation, adjustments in medication, and natural progression of the disease [9 47–49], apart from premorbid personality traits and e.g. the pre-operative psychosocial status of the individual [47], especially when DBS is used in patients with neurodegenerative disorders where changes to PIAAAS are naturally inevitable regardless of treatment course and choices. For instance, although Parkinson's disease is usually associated with motor symptoms such as bradykinesia, rest tremor, muscular rigidity, and postural instability, a large proportion of affected individuals also exhibit cognitive impairment and psychiatric symptoms [50]. Studies show that almost 25.2

to 40% of Parkinson's disease patients suffer from depression, up to 43% have anxiety disturbances, 32 to 42% exhibit apathy, 5.6 to 11.1% experience mania or hypomania, 15% have symptoms of impulse control disorders [51, 52], up to 75% complain of insomnia [53], 8 to 40% experience psychosis [54], and as many as 78.2% develop dementia [55]. Some of these disorders such as depression, anxiety disorders, apathy, and cognitive impairment might be due to the degeneration of brain structures leading to complex brain signalling disturbances caused by Parkinson's disease itself [51, 56, 57], whereas others such as mania/hypomania, impulse control disorders, and psychosis might, to a greater degree, result from dopaminergic medication used to treat motor symptoms [52, 53]. Most of these disorders are associated with multiple risk factors, and their onset and progression are determined by a combined effect of genetic susceptibility, neural degeneration, neurotransmitter dysregulation, co-existing psychiatric disorders, and medication dosage and regime [54, 58, 59]. Hence, changes in PIAAAS following DBS should not only be attributed to the DBS target structure, surgical trajectory, and stimulation parameter, but should also take into account patient history, disease attributes, and other forms of treatment adaptations such as medication adjustments. At this point in time, it is relatively difficult to isolate the cause of these post-operative changes, though they have been associated with DBS. Connected to this point is the concern that no generalizable conclusions and recommendations should be drawn from such limited data.

Second, there is a fundamental problem with empirically investigating effects of DBS on PIAAAS. As it was outlined previously [47], there are currently only a small number of scales that are trying to measure personality-related changes (for studies investigating “agency” [60, 61]). Unfortunately, a number of these scales may generate biased and/or insufficient responses because they often refer to self-report measurements. Moreover, a majority of them are test-psychologically inappropriately verified (regarding all necessary measurement criteria, e.g. reliability & validity) and do not consistently take up recent insights from psychological research (i.e. they focus on explicit-deliberate processing entirely). Finally, they rarely take up responses from third parties (e.g. spouses, relatives) that could substantially contribute to our understating of undesired changes following DBS interventions. Consequently, there are currently only vague objective markers of e.g. personality (gathered via e.g. the big five personality test) and

¹⁰ With or without marginal case reports, our position would be similar: empirical evidence suggesting a link between DBS and PIAAAS is rare. This echoes Temel et al.'s [45] meta-review where they report “personality changes, hypersexuality, apathy, anxiety, and aggressiveness were observed in less than 0.5%” of DBS outcomes “and only reported in case studies”. It is crucial to note that Temel et al. [46] do not provide specific proportion of “personality changes” within the 0.5%.

only few studies that have investigated on the topic (thereby generating only few data). Similar to the difficulties that arise when dealing with “personality” as a rich psychological concept, “identity”, “agency”, “authenticity”, “autonomy” and “self” constitute even more difficult concepts from an empirical perspective. Representing multifaceted and ambiguous constructs, these terms are far from ideal for an empirical investigation because operationalization is difficult. Whilst there are numerous studies focusing on various subsets of what could be termed “personality”, such as cognitive deterioration and changes in mood, to name a few, some of the terms related to PIAAAS seem not particularly suited for quantitative inquiries.¹¹ Because it is a vital prerequisite of empirical studies to generate concise research questions on clearly identifiable markers to meet common methodological quality criteria, it is likely that concepts such as “authenticity” and the “self” will probably remain for some time in the philosophical rather than in the empirical domain. This is not to say that with time, no better measures of PIAAAS will be developed and that investigating subsets of the latter relating to e.g. changes of affect can and will contribute to our understanding of more qualitative concepts. Also, this does not imply that ethical analysis only makes sense when neuroscience gets in that stage of complete operationalization of psychological concepts. Neuroethicists do not have to wait for neuroscience to be finished before they can contemplate on its ethical implications [28]. We are also not trying to suggest that neuroethicists can base their work only in response to neuroscientific empirical work. However, it is currently difficult to assess the degree of change to patients’ PIAAAS after DBS implantation given the scarcity of instruments to objectively assess changes of PIAAAS.

Consistent with what has been said in the previous paragraph, our third point regarding the inflation of putative effects of DBS on patient PIAAAS takes up methodological prerequisites (mostly stemming from sociology) of qualitative research. Briefly, whilst single quotes of patients can be illustrative, they need to be treated with caution. Convergence of responses representing saturation of the data should be in place before generalizing the outcome(s). Needless to say,

qualitative studies should disclose the methodological details to allow interested readers to understand them. Finally, the concept of “understanding” in qualitative research is a decisive issue that should be reviewed during the process of interviewing, analysing, and writing. Patient experiences and narratives, which should unquestionably be heard, bring fundamental knowledge to our comprehension of postoperative changes in the context of DBS. However, marginal or single case reports, do not inform us of the actual incidence of DBS-induced effects on the PIAAAS in a particular population of patients treated with DBS. In some cases, marginal or single case reports could even bend the focus in the second- and third-hand literature about changes to patient PIAAAS that, although warranting important medical and ethical consideration, could inflate potential adverse effects, way beyond what would be observed if a systematic study was conducted. Although, subjective narratives may allow to understand some aspects of the potential phenomenon of DBS-induced PIAAAS [9, 63] and some critical ethical issues, quantitative empirical studies with strong research-designs constitute an appropriate tool to investigate causal effects and to inform us about the incidence of a given variable following a certain treatment.

Finally, some have made the claim that the DBS literature does not address or publish enough negative outcomes [64–66]. If this is the case, then it would mean that the limited amount of evidence of DBS effects on patient PIAAAS may be due to lack of negative reports. In that respect, it is important to consider whether most studies have been designed to include all dimensions of DBS’s potential side effects. Should study designs neglect inclusion of subjective reports, then a lack of evidence would not be evidence of a lack; it would simply reflect that studies are not designed to capture all aspects of a potential phenomenon. Concomitantly, there is also a possibility that some patients do not report their subjective experiences. Hariz and Hamberg have observed that most implanted patients considered their side effects to be the trade-off between getting treatment and having control of the symptoms enabling them to be more active in day-to-day life while incurring with post-operative slurred speech or balance problems [67]. As well, there are no objective means of deciding when a treatment has to be considered a failure or a success [68]. Although scales and measures that can assess improvement or deterioration in certain symptoms of

¹¹ Providing evidence for empirical (correlative or causal) relations between DBS and PIAAAS might be beyond the ability of qualitative research: “Phenomenological approach cannot establish statistical relationships, because it is concerned with uniqueness and individuality, rather than numbers and statistics” [62].

neurological and psychiatric disorders exist, it is to some extent up to the patient and/or family members to decide whether the treatment is a success or not, likely on how benefits outweigh side-effects and whether they are in line with the patient's and family members' needs and expectations. It is also important to highlight that what can be deemed successful from a patient's perspective might not necessarily be deemed successful by the family. Although both the patient and family members might see relief from motor symptoms, a patient might not see potential treatment-associated hypomania as much of a nuisance as his or her family members would. This highlights that although PIAAAS changes might occur, they should not necessarily be seen as a treatment failure, automatically regarded as something completely negative, or viewed as a trade-off that a patient should not make.

Limitations of the study

A possible limitation of the study, even though simultaneously strengthening our primary claim, can be found in the practice of selectively searching for PIAAAS in the empirical literature. On the one hand, if instead of only searching for DBS, we had searched (more broadly) with terms such as neurotechnologies, brain implants, neural devices, etc., then we would have found a greater number of theoretical articles. On the other hand, as outlined previously, PIAAAS are philosophical concepts that are inherently non-scientific. Even though empirical investigations using the concepts of "personality" and "agency" do exist, they often do not fully capture the philosophical essence of these terms. For instance, autonomy is sometimes medically defined, especially in the Parkinson's literature, as the ability to perform a particular set of actions associated with daily living [69]; by comparison, the concept is portrayed more broadly in the philosophical literature. In most neuroethics and bioethics publications, the conditions for autonomy include (1) intentions (volitions), (2) competence (capacity to appreciate right and wrong and determine oneself accordingly), (3) absence of external controlling influences (freedom from external forces), and (4) absence of internal controlling influences (freedom from internal coercive influences) [70, 71]. Therefore, it is obvious that our sample of the empirical literature on PIAAAS in a wider sense is too conservative. The search terminologies we used, which are mainly based on philosophical discourse, might not have

fully captured the extent of PIAAAS-associated key words and terms as used in medical databases. Accordingly, a large number of studies were lost due to the rather narrowly defined search string. However, since the vast majority of the theoretical neuroethics literature refer to PIAAAS specifically—concepts that have weak empirical grounding—corroborates our claim that neuroethics is in danger of discussing PIAAAS-related problems without a rigorous empirical foundation; as a consequence, buying into speculative ethics. This does not mean that we neuroethicists are not allowed to take anecdotal findings in order to make a more general (thus speculative) philosophical point. However, we should accept that by not explicitly stating the weak empirical grounding of our claims, we increase the risk of inflating an empirically impenetrable speculative bubble and even more pressingly, disseminating information that might detrimentally affect the decision making of some prospective patients and their relatives who would benefit from treatment. Again, we are not advocating that philosophers should restrain from engaging in philosophically interesting theoretical reasoning stimulated by an anecdotal incident or that potential postoperative DBS changes experienced by patients are not critical ethical concern despite the low number of first-hand primary studies and large number of marginal and single case reports. Whether and in which cases philosophy should be based on empirical data, albeit an intriguing question, is not within the scope of this work. Although it is important to acknowledge the occurrence of these potential DBS-induced PIAAAS changes and to devise measures to adequately address them, they must also be viewed in light of incidence rates in order to better inform patients, family members, and caregivers of actual risk probabilities associated with this surgical intervention. Unquestionably, the measurement problem of complex changes such as PIAAAS makes the assessment of incidence rates extremely difficult, and in some cases, perhaps even impossible.

Conclusion

We have argued that there is a critical lack of primary empirical studies corroborating potential DBS-induced effects on patients' postoperative PIAAAS. We have observed a disproportionate relationship between what is available in terms of supporting empirical evidence and the number of theoretical interpretations and

assumptions canvassed by neuroethicists despite the thinness of any empirical backing of their claims concerning the impact of DBS on patient PIAAAS. To our view, this is reflective of a speculative neuroethics bubble, which may need to be deflated. Occurrences of “ethics hype” and “speculative ethics” are also discussed in other domains of ELSI literatures [72–76].

While we support the view that theoretical neuroethics is as an important field of research, we question the robustness of building philosophical accounts on limited empirical evidence (often only with very selective quotes of patient self-reports). Given the current state of the neuroethics literature as analysed in this study, most claims by neuroethicists concerning the effects of postoperative DBS PIAAAS-related changes are made up of conclusions derived from first-hand primary studies that do not include control groups, or from anecdotal reports, thereby risking that the stories seem to be ‘cherry picked’. Even if a large proportion of the published theoretical neuroethics manuscript appears to be supported by scarce data from which it is not possible to derive conclusions, potential postoperative DBS changes experienced by patients remain a critical ethical concern. Neuroethicists play a crucial role in addressing concerns of stakeholders (including patients and the general public) and improving philosophical understanding of such concepts.

However, there is a pressing and urgent need to examine the question of the effects of DBS on PIAAAS with “fresh” evidence. Publishing more first-hand primary studies can only enhance the reliability, robustness, and validity of the discipline. Epistemological and methodological challenges can be overcome by developing instruments to measure potential changes in PIAAAS. Hence, we recommend facilitating the development of instruments that will become an international standard for capturing postoperative variations in patient experience of post operative changes to PIAAAS. Responsibility to study further this question should also be taken by relevant stakeholders from the device industry, including device companies. To avoid risks of conflicts of interest(s), the stakeholder should provide necessary financial support to independent institutions to develop study protocols that will investigate more extensively issues related to DBS-associated impacts on patients’ PIAAAS.

Reading that “the risk of becoming another person following surgery is alarming” [4] and that “personality

changes represent a threat to personal identity and agency” [3] is not without consequence; particularly for prospective patients (and families) who could immediately and directly benefit from the intervention. These neuroethical assertions come with risks: they may perpetuate and propagate misleading assumptions that lack strong supportive scientific evidence. Ethics that propounds such unfounded speculation may seem to encourage the public, but most importantly prospective patients, to adopt a reluctant approach to treatment [25]. However, despite the empirical limitations, we believe investigating further these issues help patients to be informed about the potential risks of psychiatric adverse events, possible changes in personality, and other treatment-associated changes at hand. Neuroethics has a fundamental responsibility to play in articulating risks about the putative effects of DBS on PIAAAS, hence more research and funding are needed. Nonetheless, we, the neuroethicists, should also keep in mind our responsibility to properly inform our readers (potentially, prospective patients) of actual risks, acknowledging that our views are more than likely based on limited case reports. We should also work to ensure that patients and their family members are neither hyped up by overly positive depictions of DBS (notably by media), nor turned down by hyperinflated assumptions about the involved associated risks. The media account for bigger responsibilities in how the effects of DBS are portrayed to the public. Neuroscientists should receive appropriate media training so as to critically and effectively counter stories involving hype, unrealistic and inflated sensationalistic portrayals of DBS [77].

A lack of evidence of putative effects of DBS on PIAAAS is not evidence that there is no link; empirical studies are most likely not designed to capture all aspects of potential DBS-induced PIAAAS phenomena. What remains unclear is whether it is all DBS-implanted patients who are at risk of postoperative PIAAAS sequelae. Further neuroethical research is needed more than ever, especially in a context where novel generation of DBS systems including closed-loop, artificially intelligent implants, and brain-computer interfaces are being developed. [78–85] Whether or not these emerging neurotechnologies will affect PIAAAS is still uncharted territory.

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Compliance with ethical standards

Competing interests None.

Annex 1: Search Methods Employed

I. We searched the top 30 bioethics journals (according to a list provided by bioethics.net) and AJOB Neuroscience.

Name of journals:

Am J Bioethics (The American Journal of Bioethics)
 Dev World Bioeth (Developing World Bioethics)
 Hastings Cent Rep (Hastings Center Report)
 Ethnic Health (Ethnicity & Health)
 J Med Ethics (Journal of Medical Ethics)
 BMC Med Ethics (Biomed central Medical Ethics)
 Bioethics
 Neuroethics-Neth
 J Empir Res Hum Res (Journal of Empirical Research on Human Research Ethics)
 Public Health Eth-UK (Public Health Ethics)
 J Law Med Ethics (The Journal of Law, Medicine & Ethics)
 Account Res (Accountability in Research)
 J Bioethic Inq (Journal of Bioethical Inquiry)
 Med Law Rev. (Medical Law Review)
 Rev. Rom Bioeth (Revista Romana de Bioetica)
 Genet Counsel (Journal of Genetic Counseling)
 Ethik Med (Ethik in der Medizin)
 Acta Bioeth (Acta bioethica)
 Nursing Ethics
 Journal of Medicine and Philosophy
 Medicine, Health Care and Philosophy
 Nanoethics
 Theoretical Medicine and Bioethics
 The Journal of Clinical Ethics
 HEC Forum
 Cambridge Quarterly of Healthcare Ethics
 American Journal of Bioethics Primary Research
 Indian Journal of Medical Ethics
 Asian Bioethics Review

International Journal of Feminist Approaches to Bioethics
 AJOB Neuroscience.

II. Philosophy databases

Search until May 2, 2017

ProjectMuse
 JSTOR
 PhilPapers
 PhilIndex (limited search to academic journals)

III. Scientific, psychology, and psychiatry databases combined

Search until May 3, 2017

PubMed - 208 results
 Scopus - 236 results
 Embase (via Ovid) - 263 results
 Web of Science - 157 results
 PsycArticles - 17 results
 Psychology & Behavioral Sciences Collection (PBSC) - 16 results
 PsycInfo (via Ovid) - 122 results
 Psychiatry Online - 139 results (excluded news articles)

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