Leaving Users in the Dark: A Call to Define Responsibilities towards Users of Neural Implanted Devices

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Leaving Users in the Dark: A Call to Define Responsibilities towards Users of Neural Implanted Devices

Sankary et al. (2022) report the results of an empirical study on research participant experiences of exiting research at the end of clinical trials of deep-brain-stimulation (DBS) and responsive neurostimulation (RNS), in which they discuss researchers' and sponsors' obligations (e.g., regarding arrangements for follow-up care or hardware maintenance) in case of continued use of the device post-trial. In this Open Peer Commentary we will outline that a lack of arrangements for implanted neural devices also poses problems for those using these devices outside of these trials (i.e. in a clinical setting).

The possible impact of (a lack of) arrangements for users of these devices was illustrated by the experiences of respondents (n=4) that had participated in a deep-brain-stimulation (DBS) study for depression, which was ended early and abruptly without a clear plan for follow-up for participants who felt they were responding well (Sankary et al. 2022). One of the respondents described "a general sense of being dropped" (Sankary et al. 2022, 222) and respondents expressed a wish for more accountability of the sponsor, lacking information about hardware replacement costs. Other respondents that continued to use their device, but who had participated in studies with no abrupt ending, reported to expect post-trial follow-up care and sponsor-supported device hardware replacements (Sankary et al 2022). Sankary and colleagues state that in current regulations research sponsors are not prescribed obligations to facilitate continued access to investigational devices post-trial. They therefore conclude that the consent procedure should be improved and argue that, at a minimum, clinical trial

participants should be ensured to understand the level of ongoing support and follow-up care after exit from research, including any (financial) limitations (Sankary et al. 2022).

We support that the disclosure of information on (the absence of) post-trial obligations would be of value for trial participants, yet we argue that this conclusion is too limited as it fails to address the negative consequences of a lack of arrangements for neural implanted device users, including those implanted in clinical trials, as well as those implanted in (non-trial) clinical settings. The need for arrangements is illustrated by the perspectives and needs of (potential) users. Moreover, there are also moral arguments for the instalment of arrangements for users of neural implanted devices

A lack of regulations

Ancillary care and post-trial obligations emerged as topics in research ethics over the last decades (Kapumba, Desmond, and Seeley 2022). The Declaration of Helsinki (DoH) of 2000 first included a requirement for post-trial access to the "the best proven prophylactic, diagnostic and therapeutic methods identified by the study" (World Medical Association, 2000, 4) The most recent DoH states:

> In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process. (World Medical Association, 2013, 4)

The 2016 Council for International Organizations of Medical Sciences (CIOMS) guidelines state that "Addressing participants' health needs requires at least that researchers and sponsors make plans for […] providing continued access to study interventions that have demonstrated significant benefit" (CIOMS, 2016, 100-101).

Though the DoH and the CIOMS guidelines may include a moral call to provide post-trial care and/or access, they do not offer (legally) binding and concrete regulations for researchers and sponsors. White & Whittaker (2022) outline that some regulatory guidance on follow-up of trial participants involved in trials for active implantable medicinal devices can be found in European medical device regulation (REGULATION (EU) 2017/745) but argue that this guidance is "short in detail and open to interpretation by sponsors" (2). Moreover, they argue that where guidance to clarify post-trial responsibilities has been published for medicines, this is not the case for medical devices (White &Whittaker, 2022).

Post-trial access and post-trial health costs are also increasingly a topic in the scholarly debate on clinical trials in the fast-growing field of neurotechnology (Van Velthoven et al. 2022). Lázaro-Muñoz et al. (2018) for example, describe how participants having to rely on personal funds and donations for continued use of a device post-trial is the norm rather than the exception in this field, as most sponsors do not cover these costs.

Potential users' demand for arrangements

Challenges regarding (a lack of) arrangements for neural device users can be further illustrated by the case of the Argus II retinal implant, developed by Second Sight. This device, which had received FDA approval in 2013, was abruptly discontinued by the company due to financial reasons, without arrangements regarding follow-up care or maintenance of devices that were already in use (Strickland & Harris, 2022). Strickland & Harris (2022) report in IEEE spectrum that there are now 350 people around the world who may permanently lose their artificial vision in the case of a technical hiccup.

We conducted an empirical study including individual interviews with (previous) users of the Second Sight Argus II retinal chip (n=3), and a focus group with

potential trial participants of a new cortical visual neuro-implant (n=5). This study is a part of a broader empirical study consisting of three semi-structured interviews and eight focus groups that are analysed thematically. We discuss some of the preliminary results here.

One of the respondents, an Argus II retinal chip user who continued to use the device after its discontinuation, described noticing how the organization started to fall apart and realizing that no arrangements regarding follow-up care or hardware maintenance were in place. When at a later stage their device broke due to an accident, the participant was indeed without options for sponsor-supported hardware replacement. They were, quite literally, left in the dark. The respondent later stressed the importance of protocols covering what to do in case of problems (other than clinical safety issues):

> "But what are we going to do if it breaks? But also, how is the company structure set up? How do you guarantee its continued existence? […] You have to ensure that it keeps running. And if something happens, how are we going to repair it? Can it be repaired? What about insurance? Is it covered by insurance? All those questions need to be asked."

Where this respondent had received the implant in a clinical setting, Strickland & Harris (2022) also reported that individuals who had been implanted with the Argus II retinal implant during clinical trials and who continued to use the device post-trial, were without arrangements on hardware replacements.

At the same time, several of our respondents in the focus group argued that arrangements for follow-up care and hardware maintenance are conditional to even consider participation in a clinical trial for a neural implanted device. These respondents, who were potential trial participants of a new cortical visual neuro-implant, had learned about the abrupt discontinuation of the Argus II retinal implant by Second Sight, and the consequences for current users like the case described above.

They therefore argued that the sudden discontinuation of a device (e.g. due to financial reasons) without any arrangements in case of continued use of the device, even if disclosed in the informed consent process as Sankary et al propose, is a serious and unacceptable risk, requiring mitigation.

Moral arguments for arrangements

In addition, there are also moral arguments for the instalment of these arrangements. Lázaro-Muñoz et al. (2018) discuss that in a research setting, when a partial-entrustment relationship forms between consenting participants and researchers, a limited duty to care arises, which, for example, could oblige the provision of ancillary care. The authors describe three moral obligations supporting this limited duty to care, including 1) the duty to act with compassion; 2) 'respect for persons' (the duty to not treat participants simply as a means to an end); 3) participants are partners in the research enterprise (and should arguably receive more reciprocation for their participation). We found that these moral obligations were also represented in our empirical data. Respondents stressed that it should be realised that becoming blind is an emotional process and that even when results are disappointing, "there are people behind those numbers." The third moral obligation described by Lázaro-Muñez et al (2018) is further supported by the respondent in the study by Sankary et al. who expressed that a sense of reciprocity generated post-trial responsibilities. It may be argued that, based on reciprocity, the invasiveness of neural device implantation, as well as the time and energy investment required in trial participation, further increases the weight of this moral obligation.

Similarly, for neural implanted device trials in a clinical (non-trial) setting the professional responsibilities of the treating physician and their duty to care direct this moral obligation. With the implantation of the device in the patient's brain, the

neurosurgeon assumes the responsibility to care for this patient, not only for the moment of implantation, but also for the required care that follows from this implantation. Here, the locus of responsibility is clear. However, the complexity of this novel technology brings with it possible risks and harms, making the physician to an extent dependent on the organizations developing these implants to fulfil this duty to care. Additional ethical and legal procedures are required to define the web of responsibilities for the different actors is this upcoming field, including those of the developers of these devices.

Conclusion

Sankary et al. (2022) make a valuable suggestion for an improved informed consent procedure in neural device trials, aiming to inform and ensure trial participants' understanding of post-trial arrangements and the limitations. However, based on the expectations of (potential) users and moral arguments in favour of such arrangements, it becomes clear that transparency in this context is necessary, but not sufficient. Additional arrangements should be in place in order to address researchers' and physician's moral duty to care after the implantation of invasive neural implanted devices, both in clinical trials as well as in clinical (non-trial) settings. The complexity of responsibilities in this context needs further scrutiny in order to realize such arrangements for neural device users.

Within the fast-evolving field of neurotechnology, researchers, developers, medical specialists and all other stakeholders in the research ecosystem need to recognize that a new generation of implanted neural devices, for a variety of indications, comes with new challenges and responsibilities. Patients are implanted and may continue to use the implanted device if it benefits them, potentially for many years, requiring follow-up care and maintenance or replacement of hardware. Though a

number or challenges should be acknowledged when establishing arrangements for neural implanted device users (e.g. feasibility of long-term commitments of developers, both financially as well as regarding maintenance of past-generation technologies), users should not be the victim of the lack of regulations for neural implanted devices.

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