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## Ethical implications of visual neuroprostheses—a systematic review

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## PAPER

## Ethical implications of visual neuroprostheses—a systematic review

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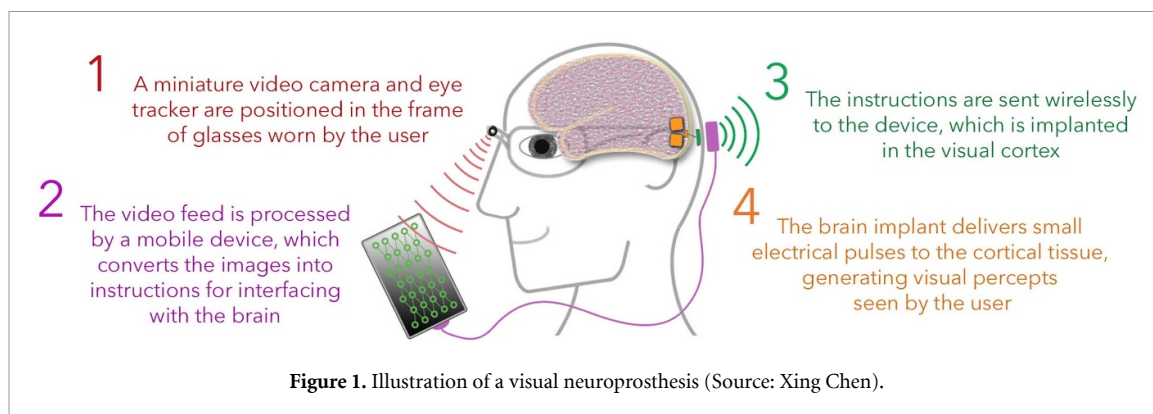
**Abstract**

**Objective.** The aim of this review was to systematically identify the ethical implications of visual neuroprostheses. **Approach.** A systematic search was performed in both PubMed and Embase using a search string that combined synonyms for visual neuroprostheses, brain–computer interfaces (BCIs), cochlear implants (CIs), and ethics. We chose to include literature on BCIs and CIs, because of their ethically relevant similarities and functional parallels with visual neuroprostheses. **Main results.** We included 84 articles in total. Six focused specifically on visual prostheses. The other articles focused more broadly on neurotechnologies, on BCIs or CIs. We identified 169 ethical implications that have been categorized under seven main themes: (a) benefits for health and well-being; (b) harm and risk; (c) autonomy; (d) societal effects; (e) clinical research; (f) regulation and governance; and (g) involvement of experts, patients and the public. **Significance.** The development and clinical use of visual neuroprostheses is accompanied by ethical issues that should be considered early in the technological development process. Though there is ample literature on the ethical implications of other types of neuroprostheses, such as motor neuroprostheses and CIs, there is a significant gap in the literature regarding the ethical implications of visual neuroprostheses. Our findings can serve as a starting point for further research and normative analysis.

**1. Introduction**

Visual neuroprostheses are sensory prostheses that can be used to restore impaired vision (see figure 1). The need for such a prosthesis is illustrated by the high global burden of disease due to impaired vision. In 2015, an estimated 36 million people were blind throughout the world, and approximately 216.6 million people had a moderate to severe visual impairment (Bourne *et al* 2017). Many causes of blindness and visual impairment, including degenerative disease, diabetic retinopathy, glaucoma or trauma, are known to have hardly any treatments.

Visual neuroprostheses have the potential to partially restore vision in these individuals (Shepherd *et al* 2013). These devices are part of the spectrum of neuroprostheses that interact with the nervous system to restore sensory or motor function (Schwartz 2004, Adewole *et al* 2016, Glannon 2016, Wright *et al* 2016). Visual prostheses aim to restore vision by targeting one of several visual processing areas, including the retina, the optic nerve, the lateral geniculate nucleus, and the visual cortex (Shepherd *et al* 2013, Lewis *et al* 2015, Mirochnik and Pezaris 2019, Niketeghad and Pouratian 2019). Research on all of these approaches is on-going, with the emergence of several clinical



trials and significant growth in the field of neuroprostheses in general over the past decade (Mirochnik and Pezaris 2019).

The development and use of visual neuroprostheses are paired with ethical implications. Some ethical implications are unique for visual neuroprostheses, while other ethical implications are applicable to neuroprostheses in general, such as the informed consent process. Some ethical implications of visual neuroprostheses are similar to those of other sensory neuroprostheses, such as some brain–computer interfaces (BCIs) and cochlear implants (CIs). CIs are a more mature technology and interact with the peripheral nervous system, and are hence accompanied by lower risks and better restoration of function. This way, they could provide a bench mark for other forms of neurotechnology.

To date, a comprehensive overview of the ethical implications of visual neuroprostheses is missing. The aim of this study is to systematically identify the ethical implications of visual neuroprostheses from the academic literature.

## 2. Methods

### 2.1. Design

In order to identify the ethical implications of visual neuroprostheses, we conducted a systematic review of the academic literature. The review process was performed following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Moher *et al* 2009). Ethical implications were broadly understood to be expressions where ethical reasons, principles and values are at stake, or any type of ethical or societal issue or consideration, which may not necessarily take the form of a fully argument-based reason (Mertz *et al* 2016).

### 2.2. Search strategy

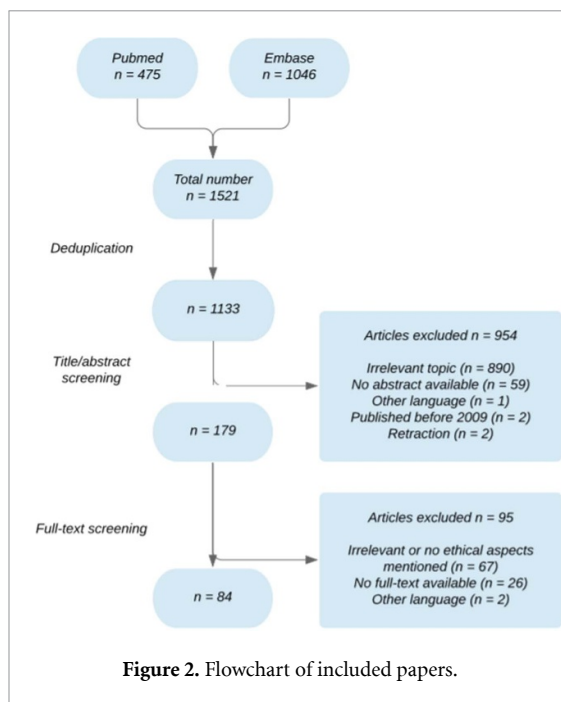
The literature search of the Pubmed and Embase databases was conducted in October 2019, and we conducted an additional search in May 2021 to include articles published since the original search. These databases were selected for their

comprehensiveness and the review's focus on medical-ethical implications. The choice of databases was discussed with an experienced librarian from the Utrecht University Library. The search strategy combined synonyms for visual prostheses, CIs, neuroprostheses, neurotechnologies, BCIs, and ethics (see supplementary files 1–4 available online at [stacks.iop.org/JNE/19/026055/mmedia](https://stacks.iop.org/JNE/19/026055/mmedia)).

### 2.3. Study selection and inclusion criteria

Articles that focused on the ethics of visual neuroprostheses, CIs, BCIs, and neurotechnologies in general were included (see figure 2). We included literature on BCIs and CIs because of ethically relevant similarities and functional parallels to visual neuroprostheses. We included literature on neurotechnology in general because of ethically relevant parallels to the field of visual neuroprostheses. We excluded articles that were not written in English or Dutch, that were published before 2009 and or lacked an abstract. In addition, articles that described very specific (sensori-motor) neurotechnologies or BCIs that were not relevant for visual neuroprostheses were excluded based on their title and abstract. For example, the ethical implications of psychiatric therapeutic applications of BCIs were considered to diverge too much from those of sensory therapeutic applications. Title and abstract-screening (tiab screening) was performed by two researchers (EAMV and KRJ).

Following tiab screening, EAMV & KRJ conducted a full-text screening of all the articles that were included (see figure 2). The results of the full-text screening were checked by a second researcher (EAMV, DRH or KRJ). We excluded articles from the full-text analysis if the full text was not available, if they discussed specific (e.g. motor-function) neurotechnologies, or BCIs that were not relevant for visual neuroprostheses, or if they did not mention any ethical issues. Only articles from peer-reviewed journals were included. In both tiab screening and full-text screening the results were juxtaposed to ensure consistency. In case of discrepancies between researchers, final inclusion was based on consensus.



## 2.4. Data extraction and analysis

A data extraction sheet was used to extract data and identify ethical implications systematically (see supplemental file 5). We extracted general information about the articles, including the author names, year of publication, country of origin, the authors' affiliations, the device or technology mentioned, and the aim of the article. The data extraction of all the articles was performed by EAMV or KJ and checked by a second reviewer (EAMV, DRH or KRJ). Discrepancies in the extracted data were discussed and resolved within the research team by consensus.

Ethical implications from all articles were then analyzed by assigning a subcode (subtheme) to each implication. Next, a list of subcodes was generated. When articles addressed the same topic, these implications were categorized under the same subcode. For each ethical implication we noted which article(s) included that topic and how many articles mentioned the particular topic. Related subcodes were categorized into main codes, in order to provide an overview of broader ethical implications. The ethical implications, subcodes and main codes were based on consensus within our research team. The formulation of these ethical implications, subcodes and main codes was re-evaluated among all the researchers several times, to ensure that all the extracted data was categorized by a code that best described the ethical implication.

## 3. Results

### 3.1. Search and selection

The database searches resulted in a total of 1521 records. After the removal of duplicates, 1133 records remained. After title screening and full-text screening,

84 articles were included for data extraction and analysis (see figure 2).

### 3.2. Characteristics of included articles

In total 84 papers were included, of which six focused specifically on visual neuroprostheses, 24 on neurotechnology in general, six on neuroprostheses in general, 27 on BCIs specifically, and 21 on CIs specifically (see table 1).

### 3.3. Ethical implications

We identified 169 ethical implications in total, which have been categorized into seven main themes: (a) benefits for health and wellbeing; (b) harm and risk; (c) autonomy; (d) societal effects; (e) clinical research; (f) regulation and governance; and (g) involvement of experts, patients and the public.

#### 3.3.1. Benefits for health and well-being

Twenty-four implications related to the theme 'Benefits for health and well-being'. An overview of these implications can be found in supplemental file 6.

First, restoration of function is often mentioned as an important health benefit. Repair and restoration of normal function is considered to be the primary goal of neuroprostheses (Tbalvandany *et al* 2019). However, while stimulation via neuroprostheses can provide some restoration of sensory function, complete restoration is not (yet) possible (Lane *et al* 2011, 2016, Laryionava and Gross 2011, Lucas 2012, Xia and Ren 2013, Rosenfeld and Wong 2017, Ereifej *et al* 2019, Wood *et al* 2019, Coin and Dubljević 2020). Moreover, several authors argued that what would be considered 'meaningful restoration' varies among people and also differs between persons who are sighted and those who are blind or visually impaired (Lane *et al* 2011, 2012, 2016, Tbalvandany *et al* 2019, Hansson 2020). Restoration of function is arguably not important to all of those who might be eligible for neuroprostheses and therefore not all of them will be interested in such restorative devices (Glannon 2016, Burwell *et al* 2017). Moreover, the literature on CIs showed that the degree of restoration of function differs between users (Kermit 2012, Pass and Graber 2015). Furthermore, measurement of the functional improvement of neuroprostheses is difficult, and should be improved by including qualitative aspects and actively involving (potential) users of the technology (Lane *et al* 2012).

Second, rehabilitation was mentioned several times in the literature. Rehabilitation and training to use a device were argued to be crucial, yet difficult or strenuous for most recipients and some might never learn to use the device (Lane *et al* 2011, Mikołajewski and Mikołajewski 2013, Xia and Ren 2013, Carmichael and Carmichael 2014, Maki-Torkko *et al* 2015, Glannon 2016, Klein 2016, Sample *et al* 2019, Thompson 2019). Functional restoration

Table 1. Characteristics of included articles.

Reference	Country of affiliation first author	Paper type	Technology	Aim of paper
Aas and Wasserman (2016)	USA	Perspective	BCIs	To argue that BCIs have an impact on attitudes towards disabilities and on norms of physical form and function.
Adams <i>et al</i> (2020)	USA	Other	Neurotechnologies	To summarize the goals of the International Brain Initiative.
Burwell <i>et al</i> (2017)	Canada	Review	BCIs	To identify and characterize the key issues associated with BCI use.
Byrd <i>et al</i> (2011)	USA	Case study	Cochlear implants	To explore the ethics of parental refusal of auditory–oral hearing rehabilitation.
Carmichael and Carmichael (2014)	UK	Perspective	BCIs	To describe current research and thinking regarding ethical issues in BCIs and brain–neural computer interfaces (BNCIs).
Carter <i>et al</i> (2019)	Australia	Other	Neurotechnologies	To summarize the goals of the Australian Brain Initiative.
Chari <i>et al</i> (2021)	UK	Review	BCIs	To outline the current state and key challenges in the field of neurotechnology, including implant technology, implant recipients, implantation methodology, implant function, and ethical, regulatory, and economic considerations.
Clausen (2013)	Germany	Review	BCIs	To present a review on ethical issues of deep brain stimulation and brain computer interfacing.
Coin and Dubljević (2020)	USA	Perspective	BCIs	To review BCI technologies and their enhancement capabilities.
DeFranco <i>et al</i> (2020)	USA	Perspective	Neurotechnologies	To provide examples and reflect on the ethical and security issues of ‘neurobioeconomy’.
Demetriades <i>et al</i> (2010)	UK	Perspective	BCIs	To present the ways in which BCIs can be used and to focus on the ethical concerns.
Duarte <i>et al</i> (2015)	Portugal	Original research	Cochlear implants	To describe the number of implants performed and to verify to what extent this is in line with the values of fairness and justice that underpin European health systems.
Echarte and Garcia-Valdecasas (2014)	Spain	Perspective	Neuroprostheses	To propose a non-deterministic and less locationist view of the Extended Mind Theory.
Ereifej <i>et al</i> (2019)	USA	Perspective	Neurotechnologies	To highlight the current state of the neural engineering field, its links with other engineering and science disciplines, and the challenges and opportunities ahead.
Farah (2015)	USA	Perspective	Neurotechnologies	To present a ‘toolbox’ of concepts for analyzing and discussing ethical dilemmas within neurotechnology.
Francis-Auton <i>et al</i> (2020)	Australia	Qualitative research	CIs	To determine whether hearing aids (HAs) or cochlear implants (CIs) are suitable for different degrees of hearing loss and in which kinds of patients.
Gladden (2017)	Poland	Perspective	Neuroprostheses	To argue that the CIA Triad provides an inadequate foundation for envisioning information security for neuroprostheses.
Glannon (2016)	Canada	Review	Neuroprostheses	To analyze and discuss ethical questions with regard to neuroprostheses.
Goering and Klein (2020)	USA	Other	Neurotechnologies	To consider several features of the BRAIN Neuroethics subgroup’s roadmap.

(Continued.)

Table 1. (Continued.)

Reference	Country of affiliation first author	Paper type	Technology	Aim of paper
Goering and Yuste (2016)	USA	Perspective	Neurotechnologies	To advocate for the early integration of ethics into neurotechnology and the development and use of these technologies.
Hansson (2020)	Sweden	Perspective	CI	To give an overview of ethical and social issues pertaining to cranial nerve implants.
Hardonk <i>et al</i> (2010)	Belgium	Qualitative Research	Cochlear implants	To examine the occurrence and importance of different factors affecting parental decisions in the choice between CIs and traditional HAs.
Hardonk <i>et al</i> (2011)	Belgium	Qualitative research	Cochlear implants	To examine factors in deaf parents' choices between CIs and traditional HAs for their child.
Haselager <i>et al</i> (2009)	The Netherlands	Perspective	BCIs	To examine ethical aspects of BCIs that are challenging for practitioners working with them.
Hendriks <i>et al</i> (2019)	USA	Review	Neurotechnologies	To provide a review of the ethical implications of neuro-modulation devices.
Hochman <i>et al</i> (2018)	Canada	Perspective	Cochlear implants	To present a single CI center's working reflections and an attempt to rationing health care decisions.
Jebari (2013)	Sweden	Review	BCIs	To review existing and emerging technologies in the field of BCIs and offer a systematic inquiry into ethical problems.
Jebari and Hansson (2013)	Sweden	Other	BCIs	To present a novel procedure used to engage the public in ethical deliberations on the potential impact of BCIs.
Jeong <i>et al</i> (2019)	Korea	Other	Neurotechnologies	To summarize the goals of the Korean Brain Initiative.
Kellmeyer (2019)	Germany	Review	Neurotechnologies	To summarize and discuss scientific, medical and ethical challenges and opportunities of automation and autonomy of artificial intelligence (AI) systems.
Kellmeyer (2018)	Germany	Perspective	Neurotechnologies	To focus on the ethical, legal and social challenges for ensuring the responsible use of 'big brain data'.
Kellmeyer <i>et al</i> (2016)	Germany	Perspective	Neurotechnologies	To analyze the effects of closed-loop medical devices on the autonomy and accountability of both people and neurotechnological closed-loop medical systems.
Kermit (2012)	Norway	Perspective	Cochlear implants	To present an overview of the bioethical debate on pediatric CIs.
Keskinbora and Keskinbora (2018)	Turkey	Review	Neuroprostheses	To analyze the ethical issues and rules with regard to 'neural dust'.
Klein (2016)	USA	Original research	BCIs	To identify key risks associated with implantable BCI research.
Klein and Ojemann (2016)	USA	Original research	BCIs	To highlight BCI research risks.
Kogel <i>et al</i> (2019)	Germany	Review	BCIs	To demonstrate approaches and concerns in considering the social impact of BCI technology.
Kotchetkov <i>et al</i> (2010)	USA	Perspective	BCIs	To discuss realistic expectations for BCI use in the military.
Kumar <i>et al</i> (2017)	India	Qualitative research	Cochlear implants	To identify parents' expectations in children with CIs.
Lane <i>et al</i> (2011)	USA	Qualitative research	Visual neuroprostheses	To report results of focus groups that were held with possible recipients of a cortical visual prosthesis.

(Continued.)

Table 1. (Continued.)

Reference	Country of affiliation first author	Paper type	Technology	Aim of paper
Lane <i>et al</i> (2012)	USA	Qualitative research	Visual neuroprostheses	To report perspectives of 30 totally blind or legally blind older individuals on their expectations for a potential visual implant, their motivations for volunteering, and their decision-making processes.
Lane <i>et al</i> (2016)	USA	Qualitative research	Visual neuroprostheses	To study and report the experiences of research participants and researchers involved in an optic nerve prosthesis project in Belgium.
Laryionava and Gross (2011)	Germany	Quantitative and Qualitative research	Neuroprostheses	To conduct an examination of discussions on neural prosthetics in German print media coverage while focusing on the public perception of ethical and social challenges.
Lazaro-Munoz <i>et al</i> (2018)	USA	Commentary	BCIs	To comment that there are no clear guidelines for continued access to brain implants.
Lee (2012)	USA	Perspective	Cochlear implants	To discuss ethical and practical issues related to CIs.
Lee (2016)	Australia	Perspective	Cochlear implants	To investigate several ethical themes and wider questions of enhancement, transhumanism and posthumanism.
Leuthardt <i>et al</i> (2021)	USA	Perspective	BCIs	To present a semantic framework that describes BCIs from a procedural standpoint and its attendant clinical risk profile.
Lucas (2012)	USA	Perspective	Neuroprostheses	To discuss how neural prostheses may assist recovery for children surviving neural injury and to argue that the use of neural prosthetics in children can provide an opportunity to reframe adult-focused ethics.
Ienca <i>et al</i> (2018)	Switzerland	Perspective	Neurotechnologies	To discuss how the neuroscience community should respond to dual-use dilemmas and propose the development of a security framework.
MacDuffie <i>et al</i> (2021)	USA	Qualitative research	Neurotechnologies	To explore attitudes of members of the neural device industry and members of the general public toward ethical challenges of neurotechnology.
Maki-Torkko <i>et al</i> (2015)	Sweden	Qualitative research	Cochlear implants	To examine pre-operative expectations and post-operative experiences related to CIs by CI-users and their significant others.
McCormick (2010)	USA	Perspective	Cochlear implants	To identify ethical conflicts in cochlear implantation therapy and show how ethical principles that are commonly accepted in health care ethics may guide decision making in resolving these conflicts.
Melton and Backous (2011)	USA	Review	Cochlear implants	To address four key areas of controversy in the prevention of common complications of pediatric cochlear implant surgery.
Mikolajewski and Mikolajewski (2013)	Poland	Review	BCIs	To investigate the extent to which ethical considerations in the clinical application of BCIs and associated risks are being identified.
Mitrasinovic <i>et al</i> (2018)	USA	Perspective	BCIs	To review the most recent research advances and the current host of engineering and neurological challenges that must be overcome for clinical application of BCIs.

(Continued.)

Table 1. (Continued.)

Reference	Country of affiliation first author	Paper type	Technology	Aim of paper
Miziara <i>et al</i> (2012)	Brazil	Perspective	Cochlear implants	To discuss the validity of implanting cochlear HAs in children by analyzing their vulnerability and the social/cultural implications of the procedure itself.
Moritz <i>et al</i> (2016)	USA	Original research	Neurotehnologies	To identify and overcome barriers to creating new neurotehnologies capable of restoring both motor and sensory function in individuals with neurological conditions.
Mudgal <i>et al</i> (2020)	India	Review	BCIs	To discuss the basic concept of BCIs, the applications of BCIs in different fields and practical issues related to the usability of BCIs.
Owoc <i>et al</i> (2018)	USA	Review	Cochlear implants	To provide data and expert commentary about elective CI removal that may help to guide clinical decision-making and formulate guidelines related to CI removal.
Panuccio <i>et al</i> (2018)	Italy	Review	Neurotehnologies	To describe the different types of brain repair strategies being developed in basic and clinical research, and provide a brief overview of recent advances in AI that have the potential to improve neuroprostheses.
Pass and Graber (2015)	USA	Perspective	Cochlear implants	To argue that the informed consent process for cochlear implantation must include access to deaf perspectives.
Postan (2020)	UK	Perspective	Neurotehnologies	To present a normative account of identity as constituted by embodied self-narratives in the context of neurotehnologies.
Quigley and Aylhonge (2018)	UK	Review	Neurotehnologies	To highlight advances in biotechnology and gaps in the legislation governing biotechnology.
Ramos <i>et al</i> (2018)	USA	Other	Neurotehnologies	To summarize the goals of the NIH Brain Initiative.
Reilly (2020)	USA	Perspective	BCIs	To outline ethical issues with BCIs from a Catholic perspective.
Rosenfeld and Wong (2017)	Australia	Review	BCIs	To give an overview of the current and future applications of neurobionics and BCIs.
Sample <i>et al</i> (2019)	Canada	Perspective	BCIs	To understand how BCIs may harm or help the user, and to investigate whether ethical guidance is needed.
Schermer (2009)	The Netherlands	Perspective	BCIs	To focus on the effects that new neurotehnologies may have on our 'symbolic order' and on the ways in which popular categories and concepts may change or be reinterpreted because of emerging neurotehnologies.
Stieglitz (2019)	Germany	Original research	Neurotehnologies	To review different stakeholders' opinions and expectations, compile information on the state-of-the-art in medical neurotehnology and describe and assess the technologies that are used to build these neurological implants.

(Continued.)



Table 1. (Continued.)

Reference	Country of affiliation first author	Paper type	Technology	Aim of paper
Sullivan <i>et al</i> (2018) Tbalvandany <i>et al</i> (2019)	USA The Netherlands	Qualitative research Perspective	Neurotechnologies BCIs	To gain a better understanding of practical and theoretical issues for end users. To examine neuro-engineering users' experiences and create guidelines to aid use of the device by the patient.
Teagle (2012) Thébaud (2013)	USA France	Perspective Perspective	Cochlear implants Cochlear implants	To outline the advantages of CIs. To assess dilemmas arising from adaptive preferences in bilateral cochlear implants for deaf children.
Thompson (2019)	USA	Perspective	BCIs	To argue that BCI illiteracy does not fully account for poor user performance in BCI systems.
Tracey and Flower (2014)	UK	Perspective	Neurotechnologies	To discuss the application of neurotechnology in a military context and its practical and ethical considerations.
Vaughan and Wolpaw (2011)	UK	Other	BCIs	To report the outcomes of the Fourth International Brain-Computer Interface Meeting.
Vieira <i>et al</i> (2018)	Brazil	Qualitative research	Cochlear implants	To understand the benefits of cochlear implantation in adulthood from the perspective of users.
Vlek <i>et al</i> (2012)	The Netherlands	Other	BCIs	To report the results of a panel that identified ethical issues related to BCIs in four case scenarios during the 4th International BCI meeting and illustrate where treatment and research interests conflict, and ethical concerns arise.
Weisleder (2012)	USA	Other	Visual neuroprostheses	To present interviews with three representatives for the blind regarding 'blind culture'.
Wolbring (2013)	Canada	Other	Cochlear implants	To present the views of members of the World Federation of the Deaf on potential human enhancement applications of CIs, and to analyze what guidance is provided for 'hearing enabling professions' in the code of ethics, regarding these potential applications.
Wood <i>et al</i> (2019)	USA	Review	Visual neuroprostheses	To discuss current and future innovations in retinal biotechnology.
Wurzman <i>et al</i> (2017)	UK	Perspective	Neurotechnologies	To argue that neuro-SciFi triggers discussions on sociopolitical and cultural phenomena and influences technological development.
Xia and Ren (2013)	China	Review	Visual neuroprostheses	To discuss several challenges in volunteer recruitment for visual prosthesis trials.
Zehr (2015)	Canada	Perspective	Neurotechnologies	To address the limitations of current technological constructs on the accepted range of human performance ability and provide a cautionary view and reflection on where our science may take the entire species.

comes with the challenge of adjusting to novel senses and experiences (Glannon 2016) and despite extensive user training, BCIs can be frustratingly slow (Sample *et al* 2019). Others mentioned that the incorporation of a device requires regained functionality and trust in the tool (Tbalvandany *et al* 2019). Furthermore, intensive training may impose time, physical, emotional, and financial burdens on the user and their family (Byrd *et al* 2011, Pass and Graber 2015, Burwell *et al* 2017). Hence, further clinical research on training and rehabilitation of patients with neuroprostheses is needed (Mikołajewski and Mikołajewski 2013).

Third, specific ethical implications for restoration and rehabilitation were raised regarding children. The CI literature, for example, suggested that early implantation of CIs in children may increase the chance of restoration, hence the option of postponing surgery until a child can make its own decisions requires a careful weighing of benefits and risks (Hardonk *et al* 2010, 2011, McCormick 2010, Byrd *et al* 2011, Melton and Backous 2011, Lucas 2012, Teagle 2012, Lee 2016, Owoc *et al* 2018). Furthermore, rehabilitation challenges faced by children with CIs are more severe than those faced by adults. Where rehabilitation challenges of CIs in adults are primarily to learn to hear again, children are faced with additional challenges, such as having to learn how to demonstrate various competences (e.g. social and linguistic) as they develop (Kermit 2012). Moreover, the rehabilitation process following CI implantation may impact the child's self-perception (Kermit 2012). Support from family members and parents is considered to be crucial for successful (re)habilitation of children (Kumar *et al* 2017).

Fourth, various authors mentioned benefits of neuroprostheses in well-being. For example, authors argued that the ultimate goal of neuroprostheses is to give the patient the feeling of 'belonging somewhere again, as being part of life' (Slatman as cited by Tbalvandany *et al* 2019, p 239). Other authors noted that users of neuroprostheses report increased life satisfaction (Maki-Torkko *et al* 2015, Kogel *et al* 2019). Neuroprostheses were argued to improve quality of life in terms of independence, pleasure, and social and emotional abilities (Hardonk *et al* 2010, Byrd *et al* 2011, Laryionava and Gross 2011, Teagle 2012, Mikołajewski and Mikołajewski 2013, Maki-Torkko *et al* 2015, Lee 2016, Burwell *et al* 2017, Vieira *et al* 2018). BCIs were mentioned to contribute to well-being by enhancing communication (Sample *et al* 2019). Yet, in the case of CI implantation in children, well-being could also be negatively affected. Concerns were expressed that when normal hearing levels are not fully attained, children may suffer comparing themselves to children with normal hearing (McCormick 2010). Some users of CIs may request device removal, due to dissatisfaction with the technology (Owoc *et al* 2018). For visual prostheses, one

paper mentioned that psychological, social, and cultural factors associated with vision have to be considered together with the ability to see, in order to assess the overall value of the prosthesis (Glannon 2016).

Lastly, CIs are argued to improve one's sense of safety- for example, by allowing CI users to pick up auditory cues from their surroundings (Byrd *et al* 2011, Maki-Torkko *et al* 2015, Vieira *et al* 2018).

### 3.3.2. Harm and risk

Aside from benefits for health and well-being, the use of visual neuroprostheses comes with potential risks. An overview of 34 implications identified in the literature can be found supplemental file 7.

First, side-effects and unintended effects were mentioned. Implantation of a neuroprosthesis comes with mechanical harms and bio-compatibility risks, including foreign body reactions such as inflammation, encapsulation, and glial scarring (Demetriades *et al* 2010, Kotchetkov *et al* 2010, Xia and Ren 2013, Klein 2016, Klein and Ojemann 2016, Moritz *et al* 2016, Burwell *et al* 2017, Rosenfeld and Wong 2017, Mitrasinovic *et al* 2018, Ereifej *et al* 2019, Stieglitz 2019, Chari *et al* 2021) and surgical risks such as haemorrhage, local damage, epilepsy and infections (Demetriades *et al* 2010, Lane *et al* 2011, Klein 2016, Moritz *et al* 2016, Burwell *et al* 2017, Lazaro-Munoz *et al* 2018, Hendriks *et al* 2019, Hansson 2020, Mudgal *et al* 2020, Reilly 2020, Leuthardt *et al* 2021). Furthermore, the heat produced by the device is a potential risk for thermal damage to the brain (Klein and Ojemann 2016, Mitrasinovic *et al* 2018, Stieglitz 2019). Aside from mechanical harm and bio-compatibility issues, there may also be other side-effects and unintended effects of implantation. Neuroprostheses may have an impact on brain function or on other health problems (Lane *et al* 2012, Chari *et al* 2021). Furthermore, users may experience psychological difficulties due to changes in their life after implantation with a sensory neuroprosthesis (Lane *et al* 2011, 2012, Xia and Ren 2013, Glannon 2016, Klein 2016, Francis-Auton *et al* 2020, Hansson 2020). Furthermore, some authors are worried that users of neuroprostheses may experience changes in personality (Schermer 2009, Laryionava and Gross 2011, Lane *et al* 2012, Jebari and Hansson 2013, Mikołajewski and Mikołajewski 2013, Goering and Yuste 2016, Moritz *et al* 2016, Mudgal *et al* 2020). However, one author argued that such statements about personality changes due to neurotechnology may be exaggerated and should not be taken at face value (Hansson 2020). Others were concerned that neuroprostheses could affect one's sense of self, thereby raising questions about authenticity (Echarte and Garcia-Valdecasas 2014, Kellmeyer *et al* 2016, Lee 2016, Moritz *et al* 2016, Burwell *et al* 2017, Carter *et al* 2019, Sample *et al* 2019, Postan 2020, Reilly 2020). Furthermore, neuroprostheses

may potentially be abused, in the sense that they may be used for harmful purposes or become difficult to control (Schermer 2009, Demetriades *et al* 2010, Kotchetkov *et al* 2010, Mikołajewski and Mikołajewski 2013, Xia and Ren 2013, Keskinbora and Keskinbora 2018, Hendriks *et al* 2019, DeFranco *et al* 2020, Hansson 2020). Similarly, the possibility of dual use, the application of neuroprostheses for non-therapeutic purposes, such as the use of neurotechnology for military combat applications, may be hard to control and even be harmful (Demetriades *et al* 2010, Kotchetkov *et al* 2010, Tracey and Flower 2014, Farah 2015, Goering and Yuste 2016, Ienca *et al* 2018, DeFranco *et al* 2020).

Second, the stability and quality of the device may pose an ethical challenge. The devices that are currently available may lose functionality over time (Kotchetkov *et al* 2010, Lucas 2012, Klein 2016, Klein and Ojemann 2016, Lane *et al* 2016, Moritz *et al* 2016, Burwell *et al* 2017, Rosenfeld and Wong 2017, Mitrasinovic *et al* 2018, Erefej *et al* 2019, Stieglitz 2019, Chari *et al* 2021) and the stability of these devices requires batteries with a long lifespan (Maki-Torkko *et al* 2015, Mitrasinovic *et al* 2018, Stieglitz 2019). Due to technological limitations of existing interfaces, retinal implants may only offer very coarse vision (Wood *et al* 2019) and difficulty hearing in the presence of background noise was frequently reported to be a shortcoming of CIs (Maki-Torkko *et al* 2015). Furthermore, explantation or re-implantation may be necessary in case of infection, decreased performance, technological failure or technological updates (McCormick 2010, Hochman *et al* 2018, Owoc *et al* 2018, Hendriks *et al* 2019, Hansson 2020). Removal of a neuroprosthesis comes with safety concerns (Owoc *et al* 2018, Wood *et al* 2019, Leuthardt *et al* 2021), and it is not known how the user may be affected by explantation of the neuroprosthesis (Lane *et al* 2012, Pass and Graber 2015, Burwell *et al* 2017, Hansson 2020).

Third, device manufacturers may introduce biases into the devices that they develop, which may lead to potential harm and unequal outcomes for patients and research (Glannon 2016, Hendriks *et al* 2019, Hansson 2020).

Fourth, privacy issues form an important aspect of the harm and risks that surround neuroprostheses. Privacy issues depend on the type of neuroprostheses being used (Gladden 2017). Several authors mentioned that neuroprostheses require proper security with regard to information privacy, encryption, and data protection (Jebari and Hansson 2013, Klein 2016, Moritz *et al* 2016, Burwell *et al* 2017, Gladden 2017, Ienca *et al* 2018, Kellmeyer 2018, 2019, Hendriks *et al* 2019, Stieglitz 2019, Postan 2020, Reilly 2020, Chari *et al* 2021, MacDuffie *et al* 2021) and that interfacing between the brain and a computer

comes with the risk of abuse or hacking (Klein and Ojemann 2016, Lee 2016, Ienca *et al* 2018, Kellmeyer 2018, Quigley and Ayihongbe 2018, Hendriks *et al* 2019, Stieglitz 2019, Hansson 2020, Reilly 2020, Chari *et al* 2021). Yet, the use of privacy protection measures should be balanced against the possible benefits of neuroprostheses (Carter *et al* 2019, Hendriks *et al* 2019).

Fifth, a number of ethical implications related to epistemic uncertainty were mentioned. Various authors argued that there is quite some uncertainty and unknown risks associated with neuroprostheses: the long-term safety of neuroprostheses is poorly understood (Laryionava and Gross 2011, Vaughan and Wolpaw 2011, Jebari and Hansson 2013, Hendriks *et al* 2019, Reilly 2020) and for long term usability, further knowledge on requirements for reliable and stable devices is needed (Vaughan and Wolpaw 2011, Klein 2016, Moritz *et al* 2016, Stieglitz 2019). In addition, improvement and validation of surgical techniques for implants are required (Hansson 2020). Neuro-technological therapy and neuro-enhancement are still accompanied by many uncertainties and unknown risks (Demetriades *et al* 2010, Farah 2015, Klein 2016, Keskinbora and Keskinbora 2018, Chari *et al* 2021). For example, while wireless power transfer is emerging, much remains unknown in terms of (long-term) safety and long-term functionality (Klein 2016, Klein and Ojemann 2016, Rosenfeld and Wong 2017, Mitrasinovic *et al* 2018). One author argued that devices for therapeutic benefit should be designed in a way that mimics healthy neurodevelopment, which requires solid understanding of these mechanisms (Lucas 2012). Furthermore, the expected benefits of neuroprostheses have been suggested to lack solid evidence (Burwell *et al* 2017, Lazaro-Munoz *et al* 2018).

Sixth, issues are mentioned that relate to high expectations and hype around neurotechnology. Patients, the public, and the media may have unrealistic and high expectations of neurotechnology, which could generate false hope and have negative effects such as disappointment (Haselager *et al* 2009, Schermer 2009, Laryionava and Gross 2011, Miziara *et al* 2012, Xia and Ren 2013, Carmichael and Carmichael 2014, Maki-Torkko *et al* 2015, Burwell *et al* 2017, Kumar *et al* 2017, Rosenfeld and Wong 2017, Wurzman *et al* 2017, Sullivan *et al* 2018, Carter *et al* 2019).

Seventh, several authors mentioned the importance of the proportionality of risks and benefits of neuroprostheses (Byrd *et al* 2011, Clausen 2013, Jebari and Hansson 2013, Moritz *et al* 2016, Rosenfeld and Wong 2017, Hendriks *et al* 2019, Reilly 2020). One author remarked that a risk-benefit analysis is a complicated endeavour, as benefits and risks are hard to quantify for hearing devices (Wolbring 2013).

Last, harm and risk concerns are especially precarious when neurotechnologies are applied to children. More research is needed to better understand the long-term stability and psychological effects of neuroprostheses, as well as their implantation in a developing nervous system (Mikołajewski and Mikołajewski 2013, Pass and Graber 2015). According to the literature on CIs, CIs in children are safe and reliable (Melton and Backous 2011).

### 3.3.3. *Autonomy*

Eleven ethical aspects related to the theme ‘autonomy’ were mentioned. An overview of these implications can be found in supplemental file 8.

Autonomy is a multifaceted concept that was interpreted by various authors in different ways, using concepts such as liberty, independence and authenticity. First, neuroprostheses contribute to independence in daily life and enhance communication with others (Lane *et al* 2012, Lucas 2012, Mikołajewski and Mikołajewski 2013, Maki-Torkko *et al* 2015, Burwell *et al* 2017, Vieira *et al* 2018). For visual prostheses specifically, restoration of vision can enable a patient to move around independently (Lane *et al* 2012, 2016). Second, CIs contribute to patients’ confidence and sense of self-worth (Maki-Torkko *et al* 2015, Vieira *et al* 2018). Third, an article mentioned the contribution of neuroprostheses to the experience of liberty (Echarte and Garcia-Valdecasas 2014). Fourth, several articles argued that new neurotechnologies should support the self-determination of the user (Moritz *et al* 2016). Yet, there may also be situations in which these neurotechnologies could potentially undermine the user’s right to freedom of choice and self-determination. For example: the type and brand of implant that is available to potential implantees may be limited due to commercial agreements between clinics and device suppliers (McCormick 2010). From a more general perspective, widespread uptake of a particular neurotechnology may make it difficult for individuals to opt out (Sample *et al* 2019). Neuroprostheses may also undermine the user’s agency (Goering and Yuste 2016, Kellmeyer *et al* 2016, Carter *et al* 2019, Jeong *et al* 2019, Chari *et al* 2021). Fifth, identity in the context of autonomy was mentioned. For example, the literature on CIs suggested that restoration of hearing in CI users can serve to reconnect them with their former (hearing) self (Kermit 2012).

Last, children are particularly vulnerable because they are not (yet) autonomous (Miziara *et al* 2012, Thébaut 2013). Nevertheless, they do have certain autonomy rights, often described as their right to an open future. For example, in the case of CIs, decisions for or against the use of the devices are made by parents on their behalf, which requires careful deliberation about the child’s interests (Hardonk *et al* 2010, 2011, McCormick 2010, Byrd *et al* 2011, Miziara *et al*

2012, Teagle 2012, Duarte *et al* 2015, Lee 2016, Owoc *et al* 2018, Hansson 2020).

### 3.3.4. *Societal effects*

Visual prostheses can have far-reaching societal effects. An overview of 26 implications can be found in supplemental file 9.

First, neurotechnology can affect social participation. Several authors mentioned that restoration through neurotechnology contributes to social participation (Lane *et al* 2012, Teagle 2012, Maki-Torkko *et al* 2015, Lee 2016)

Second, neuroprostheses could reduce the burden of care on significant others and caregivers (Lucas 2012, Maki-Torkko *et al* 2015). Yet, they can also impose extra emotional, physical or financial burdens on (significant) others (Pass and Graber 2015, Klein and Ojemann 2016, Burwell *et al* 2017, Kogel *et al* 2019). The use of neuroprostheses could alter personal relationships between patients and their loved ones, for example due to a decrease in their dependence on others (Echarte and Garcia-Valdecasas 2014, Klein and Ojemann 2016, Goering and Klein 2020). In the context of CIs, it was mentioned that parents may experience stress from having to choose whether their child should be implanted with a CI or not (Hardonk *et al* 2010).

Third, neuroprostheses influence our ideas about norms and normality. For instance, neurotechnology could alter the way in which we see ourselves, and raise questions about the relationship between humans and machines (Schermer 2009, Hardonk *et al* 2011, Laryionava and Gross 2011, Echarte and Garcia-Valdecasas 2014, Aas and Wasserman 2016, Goering and Yuste 2016, Lee 2016, Keskinbora and Keskinbora 2018, Kogel *et al* 2019, Tbalvandany *et al* 2019). Neurotechnology blurs the boundaries between humans and machines by adding ‘hybrids’ as a new category (Schermer 2009, Lucas 2012, Clausen 2013, Glannon 2016, Burwell *et al* 2017, Gladden 2017, Panuccio *et al* 2018). Furthermore, the strong focus on restoration represents a narrow account of normality that does not fit the experience of some people with a disability (Hardonk *et al* 2010, 2011, McCormick 2010, Lane *et al* 2011, 2012, Melton and Backous 2011, Lee 2012, 2016, Lucas 2012, Miziara *et al* 2012, Weisleder 2012, Jebari and Hansson 2013, Wolbring 2013, Moritz *et al* 2016, Owoc *et al* 2018, Sample *et al* 2019). For visual prostheses specifically, it was mentioned that the focus on restoration of vision may promote the perception that the life of a blind person is worth less than that of a sighted person (Lane *et al* 2012) or that disability should be understood as a social construct that only occurs when one does not have access to restorative technology (Lane *et al* 2012). With regard to stigma, some authors argued that that neuroprostheses could increase social stigmas due to differences between the bodies of neuroprostheses users and non-users

(Jebari 2013, Wolbring 2013, Aas and Wasserman 2016, Burwell *et al* 2017, Sample *et al* 2019) and that such stigma may influence the acceptance of neuroprostheses in society (Carter *et al* 2019). The use of neuroprostheses to enhance, rather than solely to restore ‘normal’ body functions, was frequently mentioned as an ethical implication (Schermer 2009, Demetriades *et al* 2010, Lane *et al* 2011, 2012, Lucas 2012, Clausen 2013, Jebari 2013, Jebari and Hansson 2013, Wolbring 2013, Farah 2015, Zehr 2015, Aas and Wasserman 2016, Kellmeyer *et al* 2016, Lee 2016, Rosenfeld and Wong 2017, Panuccio *et al* 2018, Stieglitz 2019, Coin and Dubljević 2020, Hansson 2020). Enhancement of bodily functions through neurotechnology may result in setting a ‘new normality,’ in which the position of the unenhanced individuals may be uncertain (Schermer 2009, Jebari and Hansson 2013, Mikołajewski and Mikołajewski 2013, Wolbring 2013, Farah 2015, Aas and Wasserman 2016, Lee 2016, Sample *et al* 2019). A slippery slope argument stated that the acceptance of less controversial technologies may lead to the introduction of more controversial technologies in the future (Jebari 2013). Yet, one author argued that enhancement in the context of CIs might not be a real threat, as the devices are standardized and cannot be modified at will to perform beyond the restoration of ‘normal’ hearing (Lee 2016).

Fourth, several implications related to culture were mentioned. In the literature on CIs specifically, it was mentioned that CIs were considered a threat to Deaf culture, Deaf culture was argued to be inherently valuable (McCormick 2010, Byrd *et al* 2011, Hardonk *et al* 2011, Kermit 2012, Lee 2012, 2016, Miziara *et al* 2012, Weisleder 2012, Pass and Graber 2015, Owoc *et al* 2018). Opposed to that, one author suggested that CIs are not necessarily culturally oppressive, as the decision to opt for a CI is equally culturally mediated to the argument to preserve Deaf culture (Lee 2016). With regard to visual prostheses, it was argued that the blind community may not have a ‘blind culture’ that is comparable to Deaf culture as described in the CI literature (Lane *et al* 2012, Weisleder 2012, Hansson 2020).

Fifth, several cost implications were mentioned. Neurotechnologies may be disproportionately more expensive than traditional therapy, care, and rehabilitation (McCormick 2010, Miziara *et al* 2012, Mikołajewski and Mikołajewski 2013). The development of safe neuroprostheses is expensive and requires the realization of clinically and economically viable models to realize dissemination and implementation (Vaughan and Wolpaw 2011, Stieglitz 2019). However, neurotechnologies may have a positive impact on the economy (Jebari and Hansson 2013). Furthermore, coverage by national health insurances will depend on the balance between benefit and cost (Thébaud 2013, Reilly 2020). Moreover,

as there are inter-individual differences between BCI users, a well-functioning prosthesis requires the technologies to be tailored to individual users. However, this tailoring is costly and does not benefit other users (Vlek *et al* 2012).

The last topic was accessibility of healthcare. While neuroprostheses may resolve certain social inequalities, they could give rise to new ones if devices are not affordable and access is unequal (McCormick 2010, Miziara *et al* 2012, Jebari 2013, Mikołajewski and Mikołajewski 2013, Thébaud 2013, Wolbring 2013, Glannon 2016, Goering and Yuste 2016, Rosenfeld and Wong 2017, Hochman *et al* 2018, Keskinbora and Keskinbora 2018, Sullivan *et al* 2018, DeFranco *et al* 2020, Hansson 2020, Chari *et al* 2021). On a similar note, neuroprostheses are scarce resources and therefore need to be distributed in a fair manner (Miziara *et al* 2012, Jebari and Hansson 2013, Wolbring 2013, Duarte *et al* 2015, Glannon 2016, Burwell *et al* 2017, Rosenfeld and Wong 2017, Hochman *et al* 2018).

### 3.3.5. Clinical research

An overview of 42 ethical implications in conducting clinical research on visual neuroprostheses can be found in supplemental file 10.

First, several key aspects of the informed consent process were mentioned in the literature. These implications referred to informed consent in both research and clinical settings, as was often seen in the literature on CIs. Research participants and patients need more than solely technical information when providing informed consent and differ in their information needs and preferences. Hence, sufficient time to ask questions should be provided (Lane *et al* 2011, 2016, Duarte *et al* 2015, Maki-Torkko *et al* 2015, Klein and Ojemann 2016, Rosenfeld and Wong 2017, Hendriks *et al* 2019, Francis-Auton *et al* 2020).

Furthermore, risks and possible benefits have to be explained carefully in the informed consent process of a research trial or clinical procedure (Hardonk *et al* 2011, Lane *et al* 2012, 2016, Hendriks *et al* 2019, Jeong *et al* 2019, Hansson 2020). Also, research participants consider ancillary and due care to be important aspects of the consent process (Lane *et al* 2011, 2012, 2016). Beliefs about normality and enhancement should be included in the informed consent process, because these may influence the perception of parties involved in care and policy-making, including medical insurance companies (Klein 2016). Due to the degree of complexity and amount of information relevant for the informed consent process, multiple information sessions are recommended to ensure that the research participant has understood the information (Lane *et al* 2012, Xia and Ren 2013, Klein and Ojemann 2016). Yet, epistemic uncertainties surrounding neuroprostheses can make it difficult to provide sufficient and understandable

information within the informed consent process in both research trials and clinical procedures (Kermit 2012, Vlek *et al* 2012, Xia and Ren 2013, Klein 2016, Klein and Ojemann 2016). It was mentioned that parents generally rely on information provided by medical experts when deciding whether to implant their child with a CI (Hardonk *et al* 2010, 2011). Others favored the 'reasonable person standard' for the informed consent process (information that a reasonable person may need to make an informed decision should be included), and insisted that the informed consent process in the context of CIs requires access to the testimony of patient experiences (Pass and Graber 2015). Some authors argued that potential research participants may want to involve significant others or consult other patients on their decision to participate in a research trial (Lane *et al* 2011, 2012, 2016). Furthermore, it has been argued that consent of significant others should also be sought, as neurotechnologies also affect them (Klein and Ojemann 2016). The literature also described that it is important that the informed consent process prepares participants for the potential disruption of agency and identity (Klein 2016, Klein and Ojemann 2016). Regarding factors that may influence the informed consent process, it was argued that pervasive attitudes about disability and stigma may be oppressive and thereby influence voluntary informed consent (Klein 2016). Also, unrealistic expectations about neuroprostheses can hamper informed decision-making and can lead to therapeutic misconception (Vlek *et al* 2012, Carmichael and Carmichael 2014, Klein 2016, Klein and Ojemann 2016, Burwell *et al* 2017). Furthermore, potential benefits and risks of participation in clinical trials and clinical procedures (including cultural and psychological aspects) should be carefully weighed, especially when the research participant or patient is a child (Byrd *et al* 2011, Lucas 2012, Mizziara *et al* 2012, Chari *et al* 2021).

Second, several motivations of participants in research trials were described. Some referred to personal reasons. For example, participants may consider research participation to be consistent with their adventurous preferences or curious and/or risk-taking nature (Lane *et al* 2011, 2012, 2016). Also, the desire for 'leaving a legacy' and being a pioneer could motivate research participation (Lane *et al* 2011, 2016). Increased access to healthcare or financial reimbursement were also mentioned as motivations for participating in clinical trials (Xia and Ren 2013). Authors mentioned that health benefits and independence can motivate participants (Lane *et al* 2011, 2012, 2016, Xia and Ren 2013). However, though the hope of receiving benefits from visual prostheses may be motivating, it may also be unrealistic (Xia and Ren 2013, Hansson 2020). Participation of children in clinical CI trials could be motivated by the parents'

hope that their deaf children would gain education or employment opportunities (Hardonk *et al* 2011). Furthermore, negative experiences, such as social stereotyping and prejudices of 'disability,' may motivate people to participate in clinical trials (Lane *et al* 2011). Guilt and desire for restoration may be poor motivations for participation as this indicates a poor adjustment to blindness (Lane *et al* 2016). Altruistic reasons, such as the wish to contribute to scientific progress, were also mentioned as motivation for research participation (Lane *et al* 2011, 2012, 2016, Xia and Ren 2013). Finally, it was argued that careful appeal to motivational factors is prudent, to prevent exploitation of potential participants (Lane *et al* 2012, Hendriks *et al* 2019, Hansson 2020).

Third, several implications for recruitment, selection and screening were described. With regards to recruitment, it was suggested that experts from different fields (e.g. neuroscience, engineering, ophthalmology and rehabilitative medicine) should be included in the recruitment process, to ensure that prosthesis implantation is indeed the best option for each patient (Xia and Ren 2013, Hendriks *et al* 2019, Chari *et al* 2021). Both participant screening and recruitment should be guided by ethical guidelines (Xia and Ren 2013). The literature also suggested that it is difficult to recruit volunteers for research trials of visual neuroprostheses, as the benefits are still uncertain (Xia and Ren 2013, Hansson 2020). Others, however, worried that candidates with severe disabilities are more likely to accept increased risks in BCI research trials, in the hopes of some minimal benefit (Burwell *et al* 2017). It was also noted that for those persons that still have some sight left, the risk of losing any remaining vision outweighs the potential benefits (Lane *et al* 2011, 2016). However, recruitment of participants with some residual vision can aid investigations of the effectiveness of the device (Lane *et al* 2016). The challenge is to balance respect for the participants' autonomy and the duty not to harm. This is particularly difficult in vulnerable groups who may be eager to participate (Lane *et al* 2011, 2012, Xia and Ren 2013, Klein and Ojemann 2016). With regards to the screening process of research participants, a psychologist should carry out an eligibility assessment to assess a candidate's suitability for the trial, including their motivation for participation, emotional state, potential impact of residual perception loss, and expectations regarding the efficacy of the device (Schermer 2009, Xia and Ren 2013, Lane *et al* 2016). Screening is critical for the success of clinical trials, especially in the early phases of such trials or when new devices are being tested (Xia and Ren 2013). Desire for withdrawal from the study always needs to be respected (Klein and Ojemann 2016). One article also stated that selection of participants should not be influenced by who is able to afford the

medical costs of participating in such trials (Glannon 2016). Others mentioned that the presence of a contraindication is not necessarily a barrier for implantation of a visual prosthesis in a therapeutic setting, but that in these early experimental stages, (fully) eligible patients are preferred, due to uncertainties of risks (Xia and Ren 2013).

Fourth, when it comes to research with no prospect of therapeutic benefit, it is sometimes difficult to determine what constitutes an acceptable risk (Hendriks *et al* 2019).

Last, several authors mentioned post-trial access and post-trial healthcare costs. Furthermore, the technology may advance at a rapid pace, and due to the invasiveness of the procedure, participants in early proof-of-concept studies may not be able to participate in future studies or benefit from the use of next-generation devices (Klein 2016, Klein and Ojemann 2016, Burwell *et al* 2017, Hendriks *et al* 2019). Some authors suggested that technical adjustments and improved technology should be offered to those implanted with older devices if feasible (McCormick 2010, Klein 2016). Ancillary care and post-trial health costs should be clearly communicated and covered by the trial budget (Klein 2016, Burwell *et al* 2017, Rosenfeld and Wong 2017, Lazaro-Munoz *et al* 2018, Ramos *et al* 2018, Hendriks *et al* 2019, Goering and Klein 2020). Ancillary care and post-trial healthcare costs may be burdensome for patients (Hendriks *et al* 2019). An ethical and regulatory framework regarding post-trial care in neural device research is argued to be urgently needed (Hendriks *et al* 2019).

### 3.3.6. Regulation and governance

Several papers stressed the need for regulation and legal and ethical guidance. An overview of the 16 implications of this main theme can be found in supplemental file 11.

First, several authors argued that legal guidance or regulation has to be in place in order to ensure the safety of neuroprostheses and to protect their users (Demetriades *et al* 2010, Jebari and Hansson 2013, Mikołajewski and Mikołajewski 2013, Tracey and Flower 2014, Glannon 2016, Burwell *et al* 2017, Kellmeyer 2018, Hendriks *et al* 2019, Sample *et al* 2019). More specifically, existing regulatory bodies and/or international regulation should ensure robust evaluation in the changing technological landscape (Jebari and Hansson 2013, DeFranco *et al* 2020, Reilly 2020, Chari *et al* 2021). Some argued that the regulation of the development of neuroprostheses should be balanced between protection of users and enablement of innovation (Jebari and Hansson 2013, Glannon 2016, Kellmeyer 2019, Chari *et al* 2021). Furthermore, neuroprostheses are thought to provide a challenge for the legal concept of personhood and related rights (Quigley and Ayihongbe 2018, Sample *et al* 2019, Chari *et al* 2021). It was argued that neuroprostheses should be legally conceptualized as a part of the body

(Schermer 2009, Sample *et al* 2019) and that the focus on neuroprostheses as an ‘object’ in regulation is too narrow and misunderstands the fact that the drive for innovation originates in the desire to improve health (Quigley and Ayihongbe 2018).

Second, ethical oversight was considered necessary for the governance of these technologies. Several articles mentioned that continuous ethical guidance and oversight is required to ensure that research is improved and to ensure that the technology fulfills societal goals (Jebari and Hansson 2013, Mikołajewski and Mikołajewski 2013, Carmichael and Carmichael 2014, Goering and Yuste 2016, Rosenfeld and Wong 2017, Carter *et al* 2019, Stieglitz 2019, DeFranco *et al* 2020). Ethical oversight of the application of neuroprostheses in children introduces specific additional questions, as traditional bioethical frameworks are argued to be insufficient (Lucas 2012). Moreover, further study is needed to guard against the potential downsides of rapid technological development (Mikołajewski and Mikołajewski 2013, Kellmeyer 2018). Individual differences between users make it challenging to develop a standardized framework for protection and oversight (Lane *et al* 2016). Furthermore, as the community working on visual restoration is small, oversight and monitoring boards may have a conflict of interest (Lane *et al* 2016). Potential conflicts of interest may also arise with the development and clinical research of neuroprostheses, due to financial interests of researchers or the influence of commercial organizations or big companies (Xia and Ren 2013, Glannon 2016, Kellmeyer 2019, Hansson 2020, Chari *et al* 2021). Additionally, some authors hinted that ethical guidance offers limited benefits, as it may not always lead to a better participant experience (Lane *et al* 2016).

Last, it was mentioned that neuroprostheses provide a challenge for both moral and legal notions of responsibility (Schermer 2009, Clausen 2013, Burwell *et al* 2017, Kellmeyer 2018, 2019, Jeong *et al* 2019, Sample *et al* 2019, Stieglitz 2019, Chari *et al* 2021) and that algorithms used in neuroprostheses may not be fully controllable, explainable or predictable (Kellmeyer *et al* 2016, Reilly 2020). Furthermore, researchers should learn about ethics during their education and training in order to ensure responsible innovation (Tracey and Flower 2014).

### 3.3.7. Involvement of experts, patients and the public

The involvement of experts, patients and the public was argued to be important throughout the development process of neuroprostheses. An overview of 16 implications can be found in supplemental file 12.

First, multidisciplinary teams were argued to be important for successful research, development and the application of neuroprostheses (Vaughan and Wolpaw 2011, Mikołajewski and Mikołajewski 2013, Carmichael and Carmichael 2014, Glannon 2016,

Goering and Yuste 2016, Klein 2016, Klein and Ojemann 2016, Moritz *et al* 2016, Rosenfeld and Wong 2017, Ramos *et al* 2018, Sullivan *et al* 2018, Carter *et al* 2019, Jeong *et al* 2019, Stieglitz 2019, Adams *et al* 2020, Chari *et al* 2021, MacDuffie *et al* 2021).

Second, the involvement of patients and the public was considered important: ethically sound translation of these technologies requires responsiveness to the needs of end-users (Lane *et al* 2011, 2016, Vaughan and Wolpaw 2011, Jebari and Hansson 2013, Xia and Ren 2013, Moritz *et al* 2016, Rosenfeld and Wong 2017, Kellmeyer 2018, Panuccio *et al* 2018, Sullivan *et al* 2018, Ereifej *et al* 2019, Sample *et al* 2019). Several articles mentioned that the knowledge and experiences of end-users are useful for the design of a neuroprosthesis device, for the design of a research study, and for informed consent (Lane *et al* 2011, 2012, 2016, Weisleder 2012, Moritz *et al* 2016, Sullivan *et al* 2018, Sample *et al* 2019). When patients are actively involved throughout the research process, their involvement has a positive effect on their experience of this research process (Lane *et al* 2016). Furthermore, researchers should include the perspectives of a group of (potential) end-users consisting of both proponents and opponents of the technology, to prevent selection bias in end-users engagement (Sullivan *et al* 2018). Empirical (qualitative) research into users' experiences, perceptions and needs with regards to neuroprosthesis usage is hardly ever conducted, resulting in a poor understanding of the bodily experience of those using these technologies (Lane *et al* 2011, 2016, Klein and Ojemann 2016, Quigley and Ayihongbe 2018, Sullivan *et al* 2018, Kogel *et al* 2019, Sample *et al* 2019, Tbalvandany *et al* 2019). Furthermore, efforts to make research participatory should strike a balance between scientific quality and benefit to participants (Lane *et al* 2011). Communication with the broader public is also important: socially acceptable design requires the involvement of the public and the development of ways to inform the public about neuroprostheses (Lane *et al* 2011, Jebari and Hansson 2013, Goering and Yuste 2016, Moritz *et al* 2016, Burwell *et al* 2017, Adams *et al* 2020). To foster realistic expectations of the public, responsible media coverage is needed (Haselager *et al* 2009, Laryionava and Gross 2011, Xia and Ren 2013, Carmichael and Carmichael 2014, Goering and Yuste 2016, Klein 2016, Moritz *et al* 2016, Burwell *et al* 2017, Sullivan *et al* 2018, Carter *et al* 2019). The literature also mentioned that the legislative process for neuroprostheses should be made transparent to the public (Jebari and Hansson 2013).

Lastly, the needs of end-users have to be understood in order to develop neuroprostheses that are acceptable to them (Lane *et al* 2011, Moritz *et al* 2016, Sullivan *et al* 2018, Ereifej *et al* 2019). As neuroprostheses affect society at large, it is important to understand public interests and perceptions of neurotechnology, to determine whether these

technologies are socially acceptable and whether the public has a realistic image of these technologies (Vlek *et al* 2012, Moritz *et al* 2016, Carter *et al* 2019, Kellmeyer 2019). Furthermore, awareness of the invasiveness and risks of neuroprostheses are important for acceptance by society (Jebari and Hansson 2013, Rosenfeld and Wong 2017). Images in movies and the media can have an influence on public attitudes towards neuroprostheses and enablement or further limitation of the technology (Wurzman *et al* 2017). Furthermore, some authors mentioned that while it remains unclear whether 'cyborgs' will (ever) be accepted by society (Zehr 2015), public perception may improve once the benefits are better understood (Lucas 2012).

## 4. Discussion

Despite an ongoing academic debate on the advancing field of neuroprostheses, this study is the first comprehensive overview of the ethical implications of visual neuroprostheses. The rapid technological advancements spark hope for further translation of these technologies to patients and society at large, for which ethical guidance is essential. In what follows, we discuss our findings in the light of existing literature on neurotechnology, reflect on the translation of these devices into society, and formulate an outlook for future research.

### 4.1. The ethics of visual neuroprostheses in the light of other neurotechnologies

Having reviewed the literature, we identified 169 ethical implications both of visual neuroprostheses and of related neurotechnologies such as CIs and BCIs.

Some of these implications are specific to visual neuroprostheses. For example, the literature on visual neuroprostheses showed that complete restoration of visual function is not yet possible, and there are still open questions as to what would be considered meaningful restoration (Lane *et al* 2011, 2012, 2016, Xia and Ren 2013, Rosenfeld and Wong 2017, Wood *et al* 2019, Coin and Dubljević 2020, Hansson 2020). Another example of a specific implication of visual neuroprostheses is their potential to increase the user's independence by enabling navigation through their environment (Lane *et al* 2012, 2016).

Other implications have been identified that are applicable to the broader field of neurotechnologies and are expected to become relevant for visual neuroprostheses, though whether and how exactly still remains to be seen. For example, some ethical implications focus specifically on children, but visual neuroprostheses are not expected to be used in children in the near future. Nevertheless, these implications may become applicable to visual neuroprostheses, if they become available to children in the coming decades. Another implication that remains poorly understood is related to personality change



(Schermer 2009, Laryionava and Gross 2011, Lane *et al* 2012, Jebari and Hansson 2013, Mikołajewski and Mikołajewski 2013, Goering and Yuste 2016, Moritz *et al* 2016, Mudgal *et al* 2020). For the visual neuroprosthesis such a change may be caused by clinical side-effects of the implantation of the neuroprosthesis in the brain, for instance due to a structural alteration or bleeding. A second, more indirect, way in which a user's personality or sense of self could be altered is related to the desired restoration of visual function. This restoration of function could result in the so-called Burden of Normality, which is often described in discussions on the adjustment of epilepsy patients to being symptom-free and the duties that come with a symptom-free life after successful (surgical) treatment (Gilbert 2012).

Still other ethical implications are generally applicable to all types of implanted neurotechnologies, for example (surgical/mechanical) risk and harm that are likely to be directly translatable to visual neuroprostheses. (Kotchetkov *et al* 2010, Lucas 2012, Klein 2016, Klein and Ojemann 2016, Lane *et al* 2016, Moritz *et al* 2016, Burwell *et al* 2017, Rosenfeld and Wong 2017, Mitrasinovic *et al* 2018, Ereifej *et al* 2019, Stieglitz 2019, Chari *et al* 2021). An implication that requires specific attention is the risk of devices losing functionality over time (Kotchetkov *et al* 2010, Lucas 2012, Klein 2016, Klein and Ojemann 2016, Lane *et al* 2016, Moritz *et al* 2016, Burwell *et al* 2017, Rosenfeld and Wong 2017, Mitrasinovic *et al* 2018, Ereifej *et al* 2019, Stieglitz 2019, Chari *et al* 2021), especially when this is a reason for explantation (McCormick 2010, Hochman *et al* 2018, Owoc *et al* 2018). This is even more important as it is currently not known how users are affected by the explantation of a neuroprosthesis (Lane *et al* 2012, Pass and Graber 2015, Burwell *et al* 2017, Hansson 2020).

A topic that has hardly been described in the literature on visual neuroprostheses, but may become prominent in the ethical guidance of these technologies, is the convergence of neuroprostheses with AI. This convergence opens up new ethical challenges and opportunities, including those of data protection, moral and legal responsibility, and autonomy (Kellmeyer 2019, Rainey *et al* 2020, Chari *et al* 2021). While it remains unclear whether AI will in fact be applied to this field and what its role will be, the enthusiasm for medical AI for image-processing indicates the potential benefits of such technologies for processing images in visual neuroprostheses (Pesapane *et al* 2018).

Though we can indeed learn from the ethical implications of the other neurotechnologies included in our review, it is equally important to acknowledge that relevant differences between these technologies may also exist. The category of visual neuroprostheses alone encompasses several different types

of devices, accompanied by their own specific set of ethical implications. For the ethical assessment and guidance of these technologies, it is important to differentiate between the different benefits and risks of these devices, as these differences may lead to different conditions under which these devices are ethically and socially acceptable.

#### 4.2. Translating visual prostheses into society

The clinical translation of these devices into society highlights the need to reflect on conditions for societal acceptability. Our review has pointed out the necessity of legal and ethical guidance in order to ensure safety and to protect potential users. The current legal framework focuses strongly on the safety of these devices and the protection of individual users (Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC; USA federal law: 21 CFR (2020) part 882: Neurological diagnostic devices). Applications of these technologies in non-medical settings -such as gaming and enhancement- remain beyond the scope of these regulations (The Royal Society 2019). Additional legal and ethical guidance is needed to ensure access to and fair distribution of these devices and foster the ethically sound and societally acceptable clinical translation of these devices. Our review indicates that further guidance is needed to ensure that oversight and monitoring boards have no conflicts of interest, due to the small size of the community involved, and that potential conflicts of interest due to the influence of commercial companies can be regulated.

Beyond the need to ensure the safety of and access to such devices, the clinical translation of visual prostheses also requires societal sensitivity and responsiveness. Ethically sound translation of these technologies requires responsiveness to end-users' needs (Jongsma and Bredenoord 2020). Given the relevance of societal perception of the acceptability of neurotechnologies and the impact that these technologies may have on society, public engagement is becoming increasingly important to foster trust and to better understand conditions for societal acceptance. Such societal debate should discuss stigma, the human-machine relationship, desirable aims, and usage of these devices—including enhancement possibilities, and the fair distribution of these relatively costly technical solutions. Importantly, the societal debate may be hampered by unrealistic images, dystopian phrases and futuristic narratives in the media. This raises a responsibility for journalists and media platforms to consider their role in the perpetuation of hypothetical scenarios that might eventually result in failed innovations (Sand 2018).

### 4.3. Strengths and limitations

This systematic review provides a comprehensive overview of the ethical implications brought forward in the academic literature on (visual) neuroprostheses. The articles were included after a thorough screening of the academic literature on the topic by two independent reviewers, based on a search strategy that was guided by experienced librarians. Nonetheless, this review has several limitations.

First, this review includes articles on neurotechnology in general, BCIs, and CIs. Some of these implications found in the broader literature may turn out to be only marginally relevant for visual neuroprostheses. Second, we have not snowballed the included literature to extend the search for other relevant papers. Third, a systematic review of this kind always involves reporter bias; a different group of researchers could have selected or grouped the included reasons in a different way. We have minimized bias by thoroughly discussing the ethical implications identified within our research team. Fourth, we did not perform a quality assessment of the included literature beyond the requirement to be published in an academic journal as there is no screening instrument available to assess the quality of normative papers. Finally, it was beyond the scope of this paper to assess the scientific validity of the implications and different applications of neuroprostheses discussed in the included articles.

## 5. Conclusion and outlook

Visual neuroprostheses have a broad range of ethical implications. Despite the rapid academic advancement, the ethical implications are rarely discussed in the academic literature. This article provides a systematic review of ethical implications of (visual) neuroprostheses as reported in the academic literature, in which lessons are also drawn from experiences with other neurotechnologies. The review includes six papers that specifically focused on visual neuroprostheses and 78 focused on other neurotechnologies. We have identified numerous ethical implications of (visual) neuroprostheses, which are categorized in seven overarching themes: benefits for health and well-being, harm & risk, autonomy, societal effects, clinical research, regulation & governance and involvement of experts, patients and the public. Our review indicates the need to differentiate between different technologies and their specific implications to assess the conditions for acceptability and the need to develop further regulation and ethical guidance for the translation of these technologies into society.

Further empirical research and normative analysis are needed to keep pace with technological advancements with regard to the development, design and application of visual neuroprostheses. This demands a multidisciplinary approach, as many different

stakeholders are involved in the field of visual neuroprostheses. Proactive scrutiny and multidisciplinary collaboration can help to turn these technological developments into successful innovations and can reshape the academic and societal debate to allow more realistic images and expectations of these technologies.

### Data availability statement


All data that support the findings of this study are included within the article (and any supplementary files).

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