

Chapter 10

Conclusions and
recommendations

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- 10.1 This report draws together a number of different neurotechnologies that differ in several ethically relevant respects. Three of the categories of interventions that we discuss utilise devices, while the fourth involves transplantation of cells. Some of these are physically invasive, others are not. Some achieve their effects by stimulating the brain; others do so by recording brain signals. These technologies occupy different points along their respective development trajectories, ranging from those still only explored in laboratory settings, to those that are already established treatments. They also span a variety of applications: not only divided by the therapeutic/non-therapeutic distinction; even within the category of therapeutic applications, technologies that treat physical and psychiatric symptoms may be distinguished from those that assist movement or communication.
- 10.2 This diversity not only entails a wide variety of actors, the development and use of these technologies also engages a complex and sometimes overlapping network of professional ethical norms, governance frameworks and statutory regulations. This multifaceted picture presents a challenge to drawing together the common threads that define the social and ethical issues raised by these novel neurotechnologies considered collectively. However, despite this diversity, one central feature which unites this wide-range of applications remains: these technologies intervene in the human brain. Without falling prey to reductive conceptions of the role of the brain in human existence, we may still acknowledge its special status: the healthy functioning of the brain plays central role in our capacities for leading fulfilling lives and for sustaining both our senses of ourselves and our close personal relationships.
- 10.3 This captures one side of the dynamic that lies at the foundation of our ethical analyses in this report: the tension between *need* and *uncertainty*. The significance of the healthy functioning of the brain in human existence gives us a powerful reason to intervene when illness or injury damages its functions. However, it similarly gives us reason to pause before intervening without good evidence that it will be safe and beneficial to do so. In part due to the newness of these technologies and in part because we still understand remarkably little about how the brain functions, there remain gaps in our understanding of the efficacy of some of these technologies, the biological mechanisms by which desired outcomes are achieved, and of their longer-term and unintended effects.
- 10.4 The discussions and recommendations of this report attempt to negotiate this tension. We suggest that a cluster of interests – safety, autonomy, privacy, equity, and trust – are engaged by the development and use of novel neurotechnologies, and that these warrant particular attention. In recognition of the challenges of protecting and promoting these interests across a wide variety of applications and contexts, we appeal to a particular set of virtues – inventiveness, humility, and responsibility. We suggest that these virtues provide a flexible and dynamic framework within which to characterise the values and outlooks that should be exemplified by a diverse range of actors, professions and organisations in striking a balance between responding to need while exercising caution.
- 10.5 We do not argue that the ethical issues raised by novel neurotechnologies (considered collectively) are unique or exceptional. Nevertheless, several cross-cutting priorities for ethical attention do arise: some owe their significance to the fact that these technologies intervene in an organ with a special status in human life; some relate to the vulnerability of prospective users; and others are attributable also to the sheer novelty of the products and techniques involved.

Cross-cutting themes

Supporting innovation while protecting patients

- 10.6 The virtue of inventiveness is crucial to research and innovation, yet manufacturers, particularly those operating as smaller enterprises, face significant economic obstacles to developing novel neurotechnologies from the laboratory into marketable products. Developers are competing for scarce investment in long, costly, and often precarious innovation trajectories. Some enterprises may fail before their products reach the stage of commercialisation. New funding partnerships may be needed to mitigate this risk and to ensure that scarce resources are directed at responsible research and innovation that targets the spheres in which therapeutic needs is most clearly identified. Inventive funding models could also be of benefit in supporting the development of neurotechnologies that are more affordable and easier to use, and thus more widely and equitably available. Effective and proportionate regulatory frameworks also serve these ends by encouraging innovation and clearly signposting the pathways to market.
- 10.7 To a great extent, the interests of patients who lack other treatment options, and the economic interests of those developing therapeutic applications of novel neurotechnologies, coincide in wanting a smooth passage for these technologies to clinical use as swiftly as possible. However, these respective sets of interests diverge if therapies reach the market without adequate and impartial scrutiny of their safety or efficacy, or if they are rendered too expensive by manufacturers' efforts to recoup high development costs. Oversight that is both effective and proportionate must protect prospective patients' interests in accessing much needed therapeutic neurotechnologies on two fronts: primarily by ensuring these technologies do not enter the clinical use until they have been demonstrated to do good rather than harm, but also by ensuring that the regulatory hurdles to reaching market are not so burdensome that they drain resources or deter investment. We have suggested that neither the regulatory framework applying to neurodevices, nor that governing neural stem cell therapies, currently achieves an optimal balance between these aims.

Providing access to novel therapies while safeguarding vulnerable individuals

- 10.8 Whenever therapeutic interventions involve invasions of patients' bodily integrity and impact significantly upon the functions of their physiology or mind it is essential to protect them as far as possible from potential harms and to ensure that any unavoidable risks are proportionate to the benefits that these patients might expect. However, many candidates for neurological interventions will, in a number of respects, be especially vulnerable. The majority of the neurotechnologies we have considered in this report represent new therapeutic or assistive approaches to conditions where patients have few or no other options available to them. Desperation potentially constrains the freedom with which patients and those close to them make decisions to undertake potentially risky or ineffective interventions. Moreover, due to the very nature of the kinds of conditions for which therapeutic applications of novel neurotechnologies are indicated, many prospective candidates for treatment lack capacity themselves to consent to interventions. They must rely on others to determine what is in their best interests. Each of these factors means that there is a particular imperative to protect the safety of, and support autonomous decision-making by, patients, research participants, and those close to them. This includes ensuring that they understand what is known, and just as importantly what is currently *unknown*, about the efficacy and risks of these technologies. It also means taking care not to characterise an intervention as someone's 'last best hope' without strong justification.
- 10.9 The number of people living with some of the most severe and treatment-resistant types of brain injury and illness, and who are the most likely candidates for neurotechnological interventions, is small. This may preclude the pursuit of large scale clinical trials to determine safety and efficacy. Due to the need to develop effective treatments, we recognise the necessity of

investigating these technologies through the experimental treatment of small numbers or even individual patients. However, in light of the vulnerability of many of these patients, a responsible approach to doing so will require supplementing the professional practices and ethical norms associated with treatment relationships with relevant practices from the clinical research paradigm.

- 10.10 Many therapeutic applications of novel neurotechnologies are likely to remain expensive, as much due to the highly skilled care required, as because of the costs of the technologies themselves. Equitable access to their potential benefits on a global scale is not yet foreseeable. This underscores the need to protect vulnerable individuals from exploitation by services offered outside well-regulated health care systems. This entails ensuring that patients do not seek treatment from private providers at home or overseas without appropriate referral routes and assurances as to the qualifications of these providers. Vulnerability takes on a somewhat different meaning in the context of the marketing of non-therapeutic services using neurodevices, where the devices are non-invasive and unlikely to pose serious health risks. Nevertheless, ineffective interventions in the brain on the basis of misleading claims abuse the trust of individual users and may undermine wider public understanding of the therapeutic applications of these technologies. Greater awareness-raising of the capacities and limitations of novel neurotechnologies is an important part of protecting trust and autonomy.

Maintaining trust and being honest about the limits of current knowledge

- 10.11 The vulnerability of some users underscores the responsibility of professionals to engage in clear and thorough information provision and counselling in their relationships with patients and research participants, and to reflect on individual circumstances and evolving understanding of these technologies. An essential element of this is humility with respect to making clear what is not known. Moreover, these efforts will only be as successful as the information available to professionals, and the wider popular conceptions of novel neurotechnologies, allow. Therefore important responsibilities accrue both to researchers (working in commercial enterprises and academia) and to journalists working in the non-specialist media to communicate realistic representations of these technologies and their capacities. We have observed there is evidence of hype (of overstating the capabilities of these technologies) in media representations that may be driven, at least in part, by a bias in academic publications towards publishing positive findings, and to public relations efforts on behalf of those working in product development. At an individual level, hype risks raising false hopes in those already dealing with the challenges of neurological or mental health disorders. At the level of innovation and commerce, it may initially help to attract investment, but overheated early expectations might not be capable of sustaining investor commitment throughout long and complex development trajectories.

- 10.12 In assessing the ethical and social impacts of novel neurotechnologies in this report, we are aware of the responsibilities of bioethics itself not to contribute to the cumulative engine of hype; for example, by engaging in speculation about the impacts of technological capabilities that are not yet realised. Non-therapeutic applications of neurotechnologies, including those enhancing human and military capacities, attract considerable interest from commentators. We have sought here to negotiate a balance between refraining from speculative ethical deliberations unsubstantiated by robust evidence of real-world applications of research in these emerging fields, whilst also avoiding being overly sanguine about ethical concerns arising from them, given the potentially wide demand for these applications if the ambitions of early research were to be realised.

Collecting evidence while preserving scientific integrity

- 10.13 Hype is by no means the only barrier to a full and robust understanding of the capabilities and limits of novel neurotechnologies. A significant factor is also the dispersed and undocumented nature of the evidence of clinical experiences of using these technologies. We have observed in this report a number of factors contributing to this: not least that many investigational uses of these technologies are taking place as experimental treatments, and that the framework under which medical devices are regulated does not itself enhance the public availability of pre- or

post-market evidence of safety (much less efficacy) of devices. The fragmented nature of manufacturers' and clinicians' professional experience and understanding of these technologies not only perpetuates the uncertainty that characterises this field, with associated detrimental impacts on clinical decision-making and informed consent. It also means that too little is known about therapeutic avenues that have already been explored, meaning that – contrary to the demands of responsible care – risky or fruitless interventions might be repeated unnecessarily.

- 10.14 Responsible research and innovation practices must not only be based in and reflect upon sound scientific evidence, they should also seek to generate and disseminate robust findings. We have recommended a number of areas in which the collection and transparency of this evidence could be improved by encouraging approaches that look beyond the standard model of conducting clinical trials. This includes support for collaborative registers to capture experiences of clinical uses of neurodevices and regulatory mechanisms for improved reporting and transparency of post-market incident data. These data will often record information about (sometimes deeply personal aspects of) individuals' lives. This has two implications for what is collected. First that we must attend to privacy and data protection sensitivities in sharing information about patients' care. Second, humility also reminds us of the value of documenting the kinds of outcomes that matter most to *patients*, which may not always be the same as those that are the chief focus for manufacturers or clinicians.

Treating brain disorders while monitoring impacts on the whole person

- 10.15 One reason why is important for registers, through which information on clinical experiences are disseminated, also to record patient-reported outcome measures is that the impacts of neurotechnologies often extend beyond their effects on physical or psychiatric health. The complex, potentially unintended, effects of DBS on patients' cognition, behaviour and mood are a striking example of this. Another is the particular detriment to well-being and autonomy that might be suffered by those who have come to rely on assistive neurotechnologies as participants in research studies, only to lose access to these at the conclusion of the study. Similarly, we recognise that when someone other than the patient takes non-consensual control of an implanted neurodevice, or intercepts and uses sensitive information collected by this device, these might be experienced as significant breaches of personal privacy or autonomy.
- 10.16 Therapies using novel neurotechnologies are not unique in their potential to alter how patients see themselves, are viewed by those close to them, or in impacting upon their relationships with and dependence upon others; many other serious health conditions will be similarly disruptive. Nevertheless, these kinds of effects warrant careful attention in the context of neurotechnologies because we are concerned with interventions in the brain, an organ that plays a particularly central role in the functioning of patients' bodies, minds, personal and professional lives. Any attempts to govern the uses of novel neurotechnologies must look beyond objectively-defined clinical outcomes and remain flexible enough to respond to individuals' personal and idiosyncratic reactions to the roles that these technologies might play in their lives.

Recommendations

Responsible research governance

- 10.17 The concept of 'responsible research and innovation' (RRI) is gaining increasing currency amongst policy makers as means to articulating the considerations necessary to secure ethically sound and scientifically robust research objectives, conduct and governance. We have suggested that RRI in the context of novel neurotechnologies comprises six key elements. These are:

- Clearly identified need;
- Securing safety and efficacy;
- Generating robust evidence;
- Continuous reflexive evaluation;
- Coordinated interdisciplinary action; and
- Effective and proportionate oversight.

These principles, alongside our ethical framework, inform the recommendations we have made in respect of the governance – understood both in terms of professional behaviours and regulatory controls – of research practices in the field of novel technologies

10.18 We have observed that there is a substantial unmet need for therapies for many kinds of brain disease or damage for which existing treatments have proved ineffective. Many of the novel neurotechnologies we consider in this report, however, have not yet reached the stage of being available as commercial applications, but are still only being used in research contexts. The ethical care of research participants is therefore a particular priority – not only with regard to their safety and autonomy, but also to avoid building false hopes where investigational interventions offer uncertain outcomes.

Guidance on sham controlled neurosurgical trials

10.19 In many circumstances, the best model for deriving the most robust evidence from clinical investigations is the randomised double-blinded controlled trial. However, one circumstance in which blinded controls may not always be appropriate is when this involves ‘sham neurosurgery’, involving surgical intervention upon a participant’s skull without the insertion of the active biological product under investigation. We suggest that ethical guidance on the use of sham neurosurgery is needed in time to inform the progression of UK clinical trials of neural stem cell therapies to Phase II in which efficacy is assessed. **We recommend that – to support decision-making by clinical investigators, sponsors and Research Ethics Committees – the Health Research Authority should develop guidance on the kinds of circumstances in which sham neurosurgery may, or may not, be an appropriate part of clinical investigations, and what post-trial obligations should hold in respect of participants assigned to the sham arm of trials.** (Paragraph 5.41)

Non-abandonment of research participants

10.20 There may be practical reasons why it might not be possible to continue to provide investigational therapeutic or assistive neurotechnologies to participants beyond the conclusion of a research study. The withdrawal of these technologies may nonetheless impact significantly on participants’ quality of life. We therefore reiterate here our recommendation from the Nuffield Council on Bioethics 2002 report *The ethics of research related to healthcare in developing countries*, that “researchers should endeavour before the initiation of a trial to secure post-trial access for effective interventions for participants in the trial and that the lack of such arrangements should have to be justified to a research ethics committee.” **In view of this we recommend that researchers should provide, as part of their submissions to Research Ethics Committees, exit strategies for circumstances in which they are unlikely to be in a position to provide patients with continued use of neurodevices beyond the conclusion of the study.** These strategies should be proportionate to the harm (or loss of benefit) to participants from withdrawal of the device. At minimum, these submissions should include what participants will be told as part of consent procedures about access to treatment beyond the study’s duration, and details of arrangements to offer appropriate counselling and support at the study’s conclusion. **We further recommend that the Health Research Authority guidance on care after research includes explicit recognition of the issues raised by the withdrawal of access to assistive technologies.** (Paragraph 5.45)

Guidance on conducting experimental treatment

10.21 The line between research and treatment is not always a clear one, particularly in an emerging field such as this where many novel neurotechnologies are investigated in experimental treatment contexts. However, treatment and research are governed under two distinct paradigms, neither of which is ideally suited to oversight of these kinds of experimental uses. **We recommend that the General Medical Council, the Health Research Authority and the Medical Research Council work together to produce guidance for clinicians pursuing experimental therapies. This would address lacunae between the regulation of research and treatment, with the aim of ensuring that experimental interventions are pursued in a responsible way that protects patients' interests, while supporting inventiveness through the generation of new knowledge in the public interest.** (Paragraph 5.60) The recommended guidance would adopt the best features of each of the treatment and research governance paradigms, while seeking to eliminate the worst. For example, the primacy of patient interests would be imported from the treatment paradigm, whilst the clinical research paradigm would recommend adopting clear investigatory protocols, including means of assessing efficacy and risk, independent ethical oversight, and robust methods of recording and sharing findings. We suggest that this guidance might usefully build on MRC's *Experimental medicine toolkit*.

Research into non-therapeutic applications

10.22 Uncertainties about the benefits and risks of novel neurotechnologies extend to non-therapeutic uses of non-invasive neurostimulation for non-therapeutic purposes. Though these technologies used in clinical settings do not present serious risks to health, their use for non-therapeutic purposes do not bring clear social benefits either. There is a need to understand better what the long-term effects of frequent private use of these devices might be, without research itself contributing to unnecessary interventions in the brain. **We recommend that institutional ethics committees reviewing research proposals for studies using neurostimulation directed at non-therapeutic ends ensure that these meet high standards of originality and rigour. The aim should be to prevent the use of poorly defined protocols and the unnecessary repetition of similar studies, and to make sure participants are informed about the limited knowledge of long-term unintended health effects.** (Paragraph 8.39)

10.23 Military personnel are subject to a disciplined regime in which the concept of freely given consent may be problematic where this applies to participation in the experimental use of new technologies. Studies involving human participants conducted on behalf of the Ministry of Defence in the UK must undergo scrutiny by the MOD Research Ethics Committees.¹⁰⁷⁷ However, in situations where the use of neurotechnologies does not constitute a formal research study, the position regarding ethical guidelines and informed consent may be more ambiguous. **We suggest that clinicians working with the armed forces may play a crucial role by exercising their duty of care to protect the welfare of personnel who may feel under pressure to participate in experimental military applications of novel neurotechnologies that carry uncertain risks and benefits.** (Paragraphs 8.87)

Understanding impacts on the developing brain

10.24 Some children already use BCI games, and it is possible that parents and educators may be interested in using non-invasive BCIs or neurostimulation for the purposes of achieving cognitive or educational benefits for children in their care. There is therefore a need to better understand the effects of these neurotechnologies on brain development during childhood. However, precisely this uncertainty means that an unqualified call to explore these questions

¹⁰⁷⁷ Defence Science and Technology (2012) *Research Ethics Committees (MODREC)*, available at: <http://www.science.mod.uk/engagement/modrec/modrec.aspx>

through interventional research involving children would be in tension with the virtues of responsibility and humility. **We therefore recommend that there is a need for observational studies of children, who are already using neurodevices for gaming, or to improve their capacities for attention or learning, to assess the benefits and risks of these interventions, including their effect on the developing brain.** (Paragraph 8.40)

Ethical education on dual-use applications

10.25 The development trajectories of many novel neurotechnologies are likely to be complex and non-linear. This means it may not always be possible to anticipate their dual-use applications (those that have both peaceful and hostile applications). The potential for the kinds of neurotechnologies we have discussed in this report to be put to dual use has been raised by some commentators. We have suggested that continuous reflexive evaluation of innovation pathways is an important element of responsible research and innovation in this field. We therefore welcome initiatives such as the Wellcome Trust funded collaborative ‘dual-use bioethics’ project, one strand of which has investigated the current provision of ethical training in undergraduate and postgraduate neuroscience curricula in the UK. **We recommend that, as part of their ethical training, those studying for a higher degree in neuroscience should be alerted to the possible dual-use implications of neurotechnologies.** (Paragraph 8.89)

Effective and proportionate oversight

10.26 The broad requirement that the regulation of any new technology should be both proportionate and effective takes on particular salience in view of the tension between need and uncertainty which potentially arises in the case of novel neurotechnologies.

Oversight of Notified Bodies

10.27 We have observed that there is insufficient oversight and scrutiny of the activities of Notified Bodies: the organisations responsible for confirming medium and high risk medical devices conform to statutory safety and performance requirements. **We welcome the European Commission’s proposals for tighter controls on Notified Bodies, but suggest that in the interests of transparency there is still a pressing need for the evidential bases on which Notified Bodies reach compliance decisions to be a matter of public record.** (Paragraph 7.27)

Reliance on equivalence data

10.28 European legislation currently permits medical device manufacturers to demonstrate the safety and performance of their device (for which marketing approval is being sought) on the basis of data pertaining to an ‘equivalent’ device that has already received marketing approval, rather than conducting their own clinical investigations. While recognising this may be a proportionate approach for some kinds of devices, it might not always be so for those that intervene in the brain. We therefore welcome the European Commission’s legislative proposals to introduce more specific criteria for the demonstration of equivalence, including the presumption that, for implantable and high risk devices, demonstration of equivalence with existing devices will “generally not be considered as sufficient justification” for relying on existing clinical data alone. **In recognition of the special status of the brain and continued uncertainty regarding the consequences of intervening in it, we recommend to the Medicines and Healthcare products Regulatory Agency that, where equivalence data are relied upon to demonstrate the regulatory conformity of a neurodevice, the condition of equivalence must be satisfied in relation to its effect, not only its purpose, performance and safety. Furthermore, clear justification for approving neurodevices on the basis of equivalence data alone must always be provided and open to public scrutiny.** (Paragraphs 7.33 and 7.47)

Post-market surveillance

- 10.29 The regulatory system that applies to medical devices in Europe places considerable emphasis on post-market surveillance as a means of ensuring the safety and performance of devices on the market. While reporting of adverse incidents by manufacturers is mandatory, health care professionals are encouraged, but not obliged, to report these. **We endorse the House of Commons Science and Technology Committee’s recommendation that a *Black Triangle Scheme*, similar to that used in the pharmaceutical sector, be introduced (especially when devices have received marketing approval on the basis of equivalence data) to signal to patients and professionals when an invasive medical devices is newly approved and to encourage incident reporting. We further recommend to the Medicines and Healthcare products Regulatory Agency that the reporting of adverse incidents involving all neurodevices by professionals should be mandatory. Information regarding adverse incidents and incident trend reports should be made publically available.** (Paragraph 7.55)

- 10.30 Risks to physical health are not the only kinds of potential harm posed to users of neurodevices. It is possible that accidental, unauthorised or malicious interference with the functioning of a device might lead to malfunctions that could impair health, patients’ confidence in their devices, or lead to the interception of sensitive personal data about health or neural activity. **We recommend that the Medicines and Healthcare products Regulatory Agency monitors the vulnerability of neurodevices to accidental, unauthorised or malicious interference, especially where these could impair health, undermine patients’ confidence in their devices, or lead to the interception of sensitive personal data about health or neural activity. Appropriately anonymised records of any such incidents should be made publically accessible.** (Paragraph 5.54)

Regulating neurostimulation devices under a medical regime

- 10.31 The preceding sets of recommendations relate to the regulation of devices that have received approval to be marketed for medical purposes. If a manufacturer seeks to market a neurodevice for *non*-medical purposes (such as improving concentration or mood in healthy users) then it will not fall within the scope of the European directives that apply to medical devices or be regulated by the Medicines and Healthcare Products Regulatory Agency. This means that these products will not necessarily be subject to the kinds of oversight appropriate to devices that intervene in the functions of the human body. However, the European Commission has proposed legislative reforms that would mean that some categories of active or invasive devices (such as equipment for delivering intense pulsed light) would be regulated as medical devices, *irrespective* of whether they are intended by the manufacturer to be used for a medical purpose. **We recommend, therefore, that in the interests of consistency and of providing effective and proportionate oversight of devices that intervene in the brain, that the European Commission consider including neurodevices that deliver TMS and TBS amongst the categories of devices that would (irrespective of their intended purpose) be regulated as medical devices and that their marketing in the UK is overseen by the Medicines and Healthcare products Regulatory Agency.** (Paragraph 8.52)

Proportionate oversight of the development of neural stem cell therapies

- 10.32 The regulatory system applying to regenerative medicine and advanced therapeutic medicine products (ATMPs - the category of products to which neural stem cell therapies belong) is very different from that for medical devices. In keeping with the invasive nature of these therapies, and the potentially higher risks of biological manipulation, there are strict requirements for pre-market clinical trials, involving ethical oversight and the involvement of a number of regulatory agencies. It has been suggested that, historically, the regulation of regenerative medicine has been subject to delays and regulatory overlap. **We welcome the recent and ongoing changes to achieve effective collaboration between the regulators responsible for overseeing regenerative medicine in the UK. We would encourage continued dialogue between**

regulators and researchers, genuine sharing of experiences, and reflexive systems of oversight in order to foster innovation while protecting patient safety. (Paragraph 7.72)

High standards of care for patients

10.33 The potential vulnerability of individuals with neurological or mental health disorders, many of whom will have no treatment options other than those offered by novel neurotechnologies, the special status of the brain in human existence and uncertainty about the unintended effects of intervening in it, together provide a particular imperative for robust ethical oversight of the treatment and care of patients.

Counselling prior to treatment

10.34 Given these combined factors, prospective patients and those close to them are likely to benefit from counselling to complement information provision by clinicians. **We recommend that those responsible for commissioning specialised services for the NHS in each of the UK countries make it a requirement that, where treatments involving invasive neurostimulation (and, in the future, neural stem cell therapies) are provided, patients must be offered the opportunity to receive independent counselling from suitably qualified professionals about the implications of these treatments.** (Paragraph 5.9)

Features of this counselling should include:

- That it is offered as part of the referral pathway before consent is given; this would be in addition to, rather than a replacement for, the provision of clinical information supporting informed consent;
- It should also be distinguished from any parallel provision of therapeutic counselling for patients with mental health disorders; and
- The counselling services recommended here would be analogous in delivery and aims to NHS genetic counselling services in that they should: be delivered by a member of an interdisciplinary health care team; be non-directive; provide information suitable to patients' individual circumstances and treatment options; and provide support to family members and others close to and caring for the patient.

NICE Interventional Procedures Guidance

10.35 The National Institute for Health and Care Excellence (NICE) plays a valuable role and fills an important gap in the regulatory structures governing the marketing of medical devices. It provides evidence-based guidance on the use of particular interventional procedures, which clearly sets out the ethical and practical responsibilities of practitioners and makes recommendations for appropriate oversight measures. However, while decisions about the practical application of NICE *Interventional procedures guidance* is determined at a local level by decision-makers such as commissioners and clinicians, they can only go so far in supporting good patient outcomes. **It is essential that the National Institute for Health and Care Excellence (NICE) continue to work with stakeholders, including patients, to maximise usefulness of its *Interventional procedures guidance* (IPG) and its application in real life settings. At present, compliance with NICE IPG is voluntary. We recommend that compliance with NICE IPG should be made compulsory within the NHS and that the Care Quality Commission is assigned the role of inspecting NHS trusts (and boards) to ensure compliance.** (Paragraph 5.24)

Patients using private services

10.36 Not all interventions using novel neurotechnologies will necessarily take place in the NHS. Private businesses already offer non-invasive neurostimulation services for conditions such as depression. We judge that the greatest risk to patients' health and well-being from the provision of services by private providers arises where practitioners do not have medical qualifications

and operate outside the governance structures of the health service and the norms of professional medical ethics. **We recommend that the relevant professional bodies, including the Association of British Neurologists and the Royal College of Psychiatrists, should work together to issue a set of guidelines to establish a benchmark for responsible professional standards in the delivery of non-invasive neurostimulation treatments. These guidelines should state those categories of neurostimulation treatment that should only be provided by a suitably qualified professional, following clinical evaluation of a patient by a doctor. The aim is to ensure that neurostimulation treatments are provided only where there are appropriate clinical indications and where individual risk factors have been assessed.** (Paragraph 5.31)

Making existing evidence transparent and accessible

10.37 Many investigations of novel neurotechnologies take place in small studies or interventions with individual patients. This presents a challenge to gathering a consolidated body of accessible and assessable evidence. We suggest that a number of measures might help to achieve this goal. This would be particularly valuable in the medical devices sector, where regulatory requirements for pre-market clinical investigations are light-touch.

Registers of clinical experience

10.38 **We recommend that professional bodies, such as the Association of British Neurologists, the Society of British Neurological Surgeons and the Royal College of Psychiatrists, work with each other and with relevant patient groups and charities to establish registers (where these do not already exist), or to improve the quality, accessibility and profile of those which already exist. These registers would gather data on clinical experiences of treatments using novel neurotechnologies, record the outcomes of these interventions, and make these publically available.** (Paragraph 5.63) As these registers would encompass a potentially wide range of different technologies and clinical uses, it is not possible to be prescriptive about their exact form or scope. However, we suggest that essential features would include:

- independent oversight to ensure the impartiality of registered data;
- robust mechanisms for protecting patient confidentiality;
- academic involvement to ensure the quality of data;
- dedicated curatorship, to ensure that the data collected is of a kind that is useful and informative to the intended users of the register, and collected and presented in ways that facilitate comparisons and meta-analyses of aggregate data;
- recording negative or inconclusive findings, as well as positive treatment outcomes; and
- capturing patient-reported outcomes as part of building a comprehensive picture of benefits and risks that includes subjective experiences.

Registers of this kind might initially cover data collected in the UK, but an aspiration to create connections with international data repositories as well would be valuable.

10.39 **We would further recommend that the findings – including negative or inconclusive outcomes – from research investigating non-therapeutic effects of novel neurotechnologies should also be included in these registers.** (Paragraph 8.41) This would mean that current evidence of benefits and unintended effects are brought together to reach the widest audience and achieve cross-fertilisation of valuable findings from therapeutic and non-therapeutic protocols. It would also help to prevent the unnecessary repetition of similar studies and to challenge and correct some of the problems associated with small sample sizes and research and reporting integrity that have been observed in some studies reporting enhancement effects of neurostimulation techniques.

Transparency of regulatory information

10.40 The lack of transparency in the European system for the regulation of medical devices can be seen as perpetuating the scarcity of evidence upon which patients, health professionals, and health care providers can take decisions about treatment using neurodevices. However, the European Commission has announced a number of changes that may improve the current situation. These include the recent establishment of a voluntary European Health Technology Assessment network (which aims to enable sharing of knowledge among Member States and facilitate assessment of which devices might contribute to efficiency gains and improved services), and the proposals to make key aspects of a new European Databank on Medical Devices (Eudamed) publically accessible and enhance the range of data it contains, including those on clinical investigations and post-market surveillance. **We welcome these proposed changes and the extent to which they would enhance the transparency of the European system. However, we suggest to the European Commission that Eudamed should aspire to a similar degree of transparency as that which operates in the US Food and Drug Administration (US FDA), the body charged with regulating medical devices in the US.** (Paragraph 7.28)

Evidence from regulation of exceptional or non-routine uses

10.41 Regulatory routes that oversee the provision of treatments (which are not approved for wider market distribution) to individuals or to small groups of patients are a welcome means of addressing unmet need. Nevertheless, there appear to be inadequate procedures for capturing and making accessible information on when and for what purpose regulatory approval has been given for the supply of medical devices and ATMPs under the regulatory routes encompassing exceptional or non-routine uses of products. This lack of information hampers understanding of the extent to which these regulatory mechanisms are used and of their value in providing patients with access to safe and effective treatments. Improved reporting mechanisms would support dissemination of valuable evidence of efficacy and risks to promote further learning. **We recommend that the Medicines and Healthcare products Regulatory Agency (MHRA) should record anonymised data on when, and for what purpose(s), approval has been given for the supply of neurodevices under exceptional use or custom made arrangements and for non-routine supply of ATMPs under the hospital exemption or Specials arrangements. In addition, we recommend that the MHRA establishes mandatory schemes by which manufacturers and clinicians report data on patient outcomes, and adverse events of resultant interventions.** (Paragraph 7.89) Even though regulatory responsibilities for overseeing the supply of these exceptional and non-routine uses of ATMPs and devices are devolved to the competent authorities in Member States, we suggest that it would nonetheless be valuable if data regarding their use and patient outcomes were also coordinated at a European level: by the European Medicine Agency (for ATMPs) and through Eudamed (for medical devices). These data should be accessible by health care providers and the public.

Protecting the interests of users in non-therapeutic contexts

10.42 Not all interventions using novel neurotechnologies are directed at therapeutic ends. Some may be offered for putative 'enhancement' purposes, for example to improve cognitive capacities or mood. The technologies used to deliver these services might not differ significantly from those used in therapeutic settings, thus the same ethical issues regarding their safe use, uncertainty about unintended long-term effects, and consent apply here too.

Industry standards for non-therapeutic services

10.43 The possible risks to customers' health from non-invasive neurostimulation for non-therapeutic ends (such as putative enhancement effects) are unlikely to be sufficient to warrant restricting consumers' freedom to undertake them. Nevertheless, the special status of the brain and the potential for hype to distort public understanding of the capacities of neurotechnologies to benefit individuals without brain disorders or damage, places a responsibility on businesses

offering services using neurodevices for non-therapeutic purposes to adhere to safe and honest practices that protect their customers' health and equip them to make informed choices about undergoing these kinds of interventions. **We recommend therefore, that service providers should form a trade association to establish and uphold best practice standards in the sector of non-therapeutic neurostimulation and neurofeedback. These standards would encompass best practice for both the delivery of interventions, and the kind of information provided to customers.** (Paragraph 8.59)

Cognitive enhancement uses in children

10.44 Where neurodevices are used for the putative purposes of cognitive enhancement, one particular area of concern is the coercive use of neurostimulation and neurofeedback in children. The effects of these interventions on the developing brain are, as yet, unclear, and children and young people may be less well equipped to resist pressures from educators or parents who wish them to use neurotechnologies to enhance their capacities for learning and educational performance. **We recommend that the departments for education in each of the governments in the UK and the Royal College of Paediatrics and Child Health should issue advice directed to both teachers and parents on the current best evidence, and the evidence gaps, of the efficacy and risks of neurofeedback and neurostimulation for cognitive enhancement in children.** (Paragraph 8.62)

Coercive interrogation uses

10.45 There is some evidence that non-invasive BCI devices have been marketed for purposes analogous to lie detection, or to ascertain whether individuals under suspicion recognise particular images or information. It has also been speculated that neurostimulation could be used in interrogation contexts. Coercive interrogation is prohibited under the Geneva Conventions and the involvement of doctors in cruel, inhuman or degrading treatment of detainees is prohibited under the Declaration of Tokyo. However, non-invasive neurostimulation devices or non-invasive BCIs do not necessarily require operation by a medical professional. **We recommend that the armed forces and intelligence services consider issuing advice to their personnel that the use of neurodevices in interrogation is coercive and as such is prohibited under international humanitarian law.** (Paragraph 8.84)

Responsible communication

10.46 Exaggerating the capacities of novel neurotechnologies and extrapolation beyond that which is supported by the available evidence risks exposing vulnerable patients, customers, prospective research participants, and those close to them to false hope and misinformation. This could interfere with their capacities to make the best decisions regarding treatment or use, and it could also undermine wider trust and understanding of therapeutic interventions in the brain.

Responsibilities of professional communicators

10.47 We endorse existing guidelines (from multiple sources)¹⁰⁷⁸ for the accurate and responsible reporting of science in general and re-emphasise their importance in communicating the capacities of novel neurotechnologies. In addition to adhering to these guidelines, **we**

¹⁰⁷⁸ For example, see: Social Issues Research Centre (2001) *Guidelines on science and health communication*, available at: http://www.sirc.org/publik/revised_guidelines.shtml#guide1; International Council for Science (2010) *Advisory note "science communication"* available at: <http://www.icsu.org/publications/cfrs-statements/science-communication/advisory-note-science-communication>; BBC Trust (2011) *BBC trust review of impartiality and accuracy of the BBC's coverage of science*, available at: http://www.bbc.co.uk/bbctrust/assets/files/pdf/our_work/science_impartiality/science_impartiality.pdf; Science Media Centre (2012) *10 best practice guidelines for reporting science and health stories*, available at: <http://www.sciencemediacentre.org/wp-content/uploads/2012/09/10-best-practice-guidelines-for-science-and-health-reporting.pdf>.

recommend that all actors working in professions involved in communicating the findings of research involving novel neurotechnologies have a responsibility to reflect upon how their representation of the current and future applications of novel neurotechnologies might impact on others and to remain circumspect about the promises of these applications (however exciting they may be to them professionally or personally). In recommending this, we have deliberately not produced a simple checklist, but instead a set of considerations that are intended to not only guide the reflections of individual actors, but also to be taken into account by institutions and professional bodies involved in the entire circuit of neurotechnology communications in drawing up professional guidance on good practice in this field. **Specifically, we recommend that these professionals and organisations should attend to the following elements of responsible communication practices:**

- to reflect on the pressures that may be imposed by institutional and structural forces to add a ‘pinch of hype’ and to consider the successive and cumulative effect of this upon on the way in which a story may enter the public domain;
- to resist pressure to publish only positive or PR-attractive findings;
- to be clear about any features of a research study’s aims, scope or methodology that might preclude generalising its findings to wider populations or to practical real-world applications, and to resist the temptation to over-claim or engage in unjustified extrapolation beyond that which is supported by research evidence. It can be as important to say what the research does not imply, as what it does. Existing guidelines (from organisations including the SMC) have highlighted a similar imperative in relation to science reporting in general; we re-emphasise it here in the context of novel neurotechnologies where investigations are often pursued through single patient interventions or small studies;
- to be transparent about the source of funding of the research reported, especially if it has been conducted on behalf of, or supported by, an organisation with a commercial interest in the findings;
- while the use of vivid language, metaphors and images are intrinsic to professional communication practices, it is nevertheless important to refrain from misusing powerful visual devices or engaging personal stories in ways that might mislead. For example, where treatment outcomes are not unequivocally positive, accounts of patients with dramatically reduced symptoms should be accompanied by the stories of those who have different experiences. It may also be important to consider how using language such as ‘promise’ or ‘therapeutic’ to describe research outcomes might undermine efforts to communicate the uncertainties or limits of this research by eliding aspirations for a technology with its current capabilities;
- where an explicit connection is made between a neurotechnology and a particular therapeutic application, to be clear not only about the kinds of conditions the intervention would address and the balance of risks to benefits for patients, but also any continuing uncertainties, including those relating to longer term outcomes. Given the likely high cost of many novel neurotechnologies and the long development trajectories of stem cell-based therapies, it is also important to reflect accurately the realistic prospects for wide availability to patients;
- to acknowledge diversity in the perspectives of patients with neurological and mental health disorders and those close to them, by recognising that novel neurotechnologies may not be the only or indisputable means of addressing their needs and that, for some, a focus on restoring lost function or ‘normalisation’ might not represent their priorities or best interests; and

- **to be aware of the broader social, legal, and political implications of research in the sensitive area of the human brain, including the ways in which the research might be applied to other domains.** (Paragraph 9.72)

10.48 Our recommendations regarding the practices and virtues that would be exemplified by responsible reporting of novel neurotechnologies by researchers, press officers, and journalists are a significant part of ensuring responsible communications. However, insofar as these recommendations are made with a particular emphasis on preventing hype, they risk futility if the other components of the engine that drives hype remain unchecked. It is neither reasonable nor desirable to excise all the reasons researchers have to be excited about and share the fruits of their inventiveness and inquiry – indeed, throughout this report, we have emphasised the need for greater dissemination of research and experimental findings. Nevertheless, in light of the problems of hype in this field **we recommend that the UK governments, higher education funding councils and universities reflect on the effects that the ‘impact agenda’ might be having on the ways in which the promises and limitations of novel neurotechnologies are communicated by academic institutions and their researchers.** (Paragraph 9.73)

10.49 **Businesses and universities developing and promoting commercial products from neurotechnological research should also reflect on their own responsibilities when seeking to publicise this research, attract funding for development, and market their products.** (Paragraph 9.74)

Concluding remarks

10.50 In this report, we have examined the diverse therapeutic and non-therapeutic purposes to which novel neurotechnologies might be applied. Where these technologies offer therapeutic benefits, they frequently represent one of the few, or only, treatment options currently available to individuals living with serious neurological or mental health disorders. There is, therefore, considerable value in inventive and reflective research and innovation practices in this field. However, this is also an area marked by uncertainty, vulnerability and hype. The virtues of responsibility and humility require that decisions – taken by professionals and patients – about undertaking interventions using novel neurotechnologies should be based on the best available evidence of their benefits and risks. This evidence is still being accumulated and we have recommended a number of ways to capitalise more effectively on existing knowledge. We have also indicated where further investigations must be governed by ethical standards appropriate to interventions in the brain. The global need for effective treatments for serious neurological conditions is substantial. Where interventions using novel neurotechnologies have been demonstrated to be safe and effective, and provided they are subject to appropriate regulatory oversight, we would hope that the exercise of inventiveness would mean that they also become cheaper, easier to use, and more widely and equitably available.