資料２

脳・神経科学研究倫理の米国大統領生命倫理諮問委員会における検討について

第87回生命倫理専門調査会
2015年2月24日（火）15:00--17:15
内閣府庁舎3階　特別会議室
樋口範雄
nhiguchi@j.u-tokyo.ac.jp

http://www.bioethics.gov/

Presidential Commission
for the Study of Bioethical Issues

Members

- Amy Gutmann, Ph.D., Chair
- James W. Wagner, Ph.D., Vice Chair
- **Anita L. Allen, J.D., Ph.D**.
- John D. Arras, Ph.D.
- Barbara F. Atkinson, M.D.
- **Nita A. Farahany, J.D., Ph.D.**
- Christine Grady, R.N., Ph.D.
- Stephen L. Hauser, M.D.
- Raju S. Kucherlapati, Ph.D.
- Nelson Lee Michael, M.D., Ph.D.
- Daniel Sulmasy, M.D., Ph.D.

History

- The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1974-78) is generally viewed as the first national bioethics commission. Established as part of the 1974 National Research Act, the National Commission is best known for the Belmont Report.
- The Presidential Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (1978-83), also established by Congress, produced reports on foregoing life-sustaining treatment and access to health care, among other topics. Its 1981 report Defining Death was the basis of the Uniform Determination of Death Act, a model law that was enacted by most U.S. states.

- The Advisory Committee on Human Radiation Experiments (1994-95)
- The National Bioethics Advisory Commission (1996-2001) examined topics including cloning, human stem cell research, and research involving human subjects. President George W. Bush established the President's Council on Bioethics (2001-2009), which issued reports on stem cell research, human enhancement, and reproductive technologies.
- President Barack Obama created the current commission by Executive Order in November 2009.

http://bioethics.gov/node/3543

- **GRAY MATTERS**
- Integrative Approaches for Neuroscience, Ethics, and Society**VOLUME 1**

- The **President's** Council **on Bioethics**
- **Washington, D.C.**
- **May 2014**
- **http://www.bioethics.gov**

- Gray Matters: Integrative Approaches for Neuroscience, Ethics, and Society is the first set of recommendations from the Bioethics Commission in response to a request from President Obama to review the ethical issues associated with the conduct and implications of neuroscience research. Specifically the President asked the Bioethics Commission to "identify proactively a set of core ethical standards – both to guide neuroscience research and to address some of the ethical dilemmas that may be raised by the application of neuroscience research findings." This volume is the first of a two-part response to the President's request and focuses on the **integration of ethics into neuroscience research across the life of a research endeavor**.

- Integrating ethics explicitly and systematically into the relatively new field of contemporary neuroscience allows us to incorporate ethical insights into the scientific process and to consider societal implications of neuroscience research from the start. Early ethics integration can prevent the need for corrective interventions resulting from ethical mishaps that erode public trust in science. **Everyone benefits when the emphasis is on integration, not intervention. Ethics in science must not come to the fore for the first time after something has gone wrong**.

- contemporary neuroscience
- 1) molecular
- 2)cognitive
- 3) clinical
- preventive
- diagnostic
- therapeutic

通常の医療倫理との相違

- data privacy
- informed consent
- minimization of risk
- **Privacy of thoughts**
- **threats to personal volition**
- **erosion of self-determination**

- **他の臓器・組織との違い**
- **personal identity を扱う部分**
- **具体的に4つの場面で検証**

1) neuroimaging and brain privacy

- CT, PET, EEG, fMRI

- 脳の動きがわかるようになってきた

- crime prevention
- lie detection
- criminal intent

- ある研究　指輪または腕時計を盗ませて、後で証言させる
- 盗まない人の脳の動き、盗んだ人の動き
- 90%の確率で、嘘を発見　ただし限界あり

2) Dementia, personality and changed preferences

- アメリカ人の240万人から550万人が認知症
- 世界では3500万人とも

- 加齢とともに増加
- 71-79歳　5%　80-89歳だと24%
- 90歳以上だと37%

- diagnostic →将来へのプランニング
- 問題:　認知症前の事前指示書　認知症の現在の指示
- どちらを優先させるか？
- いずれが本当の自己決定か
-

3) Cognitive enhancement and justice

- coffee, yoga, some stimulant drugs
- treatment for ADHD

- **treatment versus enhancement**
- **　この区分は可能か？**
- **可能だとして、後者は、justice の問題を提起する**

- **問　試験前の興奮剤の摂取　Adderall**
- **　これとドーピングとはどう異なるか**

4) Deep Brain Stimulation Research

- **DBS**
- **2002年、パーキンソン病治療に一定の成果**

- **他方でロボトミーをめぐる歴史**
- **　1940年から50年代　4万件の手術**
- **　ノーベル賞まで授与される**

- **相当の慎重さが求められる領域**
- **　guidelines**

http://neurosurgery.ucsf.edu/index.php/movement_disorders_referrals.html

- Guidelines for Referring Neurologists: Deep Brain Stimulation for Parkinson's Disease
  Who is a good candidate for deep brain stimulation for Parkinson's Disease? Guidelines for referring neurologists: The criteria that we use for offering patients DBS surgery for Parkinson's disease are as follows:
- 1. **Clear diagnosis of idiopathic PD**. Patients with atypical parkinsonism or "parkinson's plus" syndromes do not respond to DBS. If there are features in the history and physical that are suggestive of atypical parkinsonism (such as very rapid progression of symptoms, autonomic failure or postural instability as early features of the disease, signs of cerebellar or pyramidal dysfunction) or an MRI suggesting an atypical syndrome, surgery is contraindicated.

- 2. Intact cognitive function. A good screening test is the mini-mental status test. A score of >26 is ideal, < 24 an absolute contraindication. Patients with cognitive dysfunction have difficulty tolerating awake surgery, may have permanent worsening of cognitive function postoperatively, deal poorly with the intrinsic complexity of DBS therapy, and realize little overall functional gain even if motor performance is improved. In borderline cases, we obtain formal neuropsychological evaluation.
- 3. Clear evidence of motor improvement with sinemet, with good motor function in the best on-medication state. A good screening test is the Unified Parkinson's Disease Rating Scale (UPDRS) part III, performed in 12 hours off of medication and repeated following a supratherapeutic sinemet dose. We require at least a 30% improvement in this score with sinemet. The patient should be ambulatory in the best on state without much assistance. In general surgery makes the "off" states more like the "on" states but rarely does better than the best "on" state, so a patient with poor function in best "on" (for example, nonambulatory in best "on") is a poor surgical candidate. Patients who fluctuate between good motor function while "on" and poor motor function while "off" are usually good surgical candidates.

- 4. Lack of comorbidity. Serious cardiac disease, uncontrolled hypertension, or any major other chronic systemic illness increases the risk and decreases the benefit of surgery.
- 5. Realistic expectations. People who expect a sudden miracle are disappointed with the results, and become frustrated with the complexity of the therapy.

6. Patient age. The benefits of DBS for PD decline with advancing age, and the risks go up. Patients over 75 are informed that their benefits are likely to be modest. We have rarely implanted PD patients who are over 80.

7. Screening MRI of the brain should be free of severe vascular disease, atrophy that is out of proportion to age, or signs of atypical parkinsonism.

- 8. Degree of disability. DBS is a poor procedure to rescue someone with end stage PD, although these are the most desperate patients. It is also not appropriate for early PD when the symptoms are very well controlled on medical therapy. Patients should have an off-medication UPDRS-III score of > 25. The best time to intervene surgically is when the patient is just beginning to lose the ability to perform activities meaningful to him/her, in spite of optimal medical therapy. Often, this is associated with the development of significant motor fluctuations, dyskinesias, or both. In a patient who is still working, the time to intervene is before the patient is forced to retire on disability.
- 9. Ability to remain calm and cooperative during awake eurosurgerylasting about 2-3 hours per side of brain. A helpful "screening test" for this is how well the patient tolerates an MRI scan. For patients who are otherwise excellent candidates but could not tolerate being awake for part of the surgery, it is possible to have the DBS implantation under general anesthesia in our interventional MRI suite.
- 10. Willingness and ability to be seen for follow-up visits. Programming the DBS to find the optimal stimulation settings is very much a trial-and-error process, and the patient will need to be seen approximately once a month for at least the first few months after surgery.

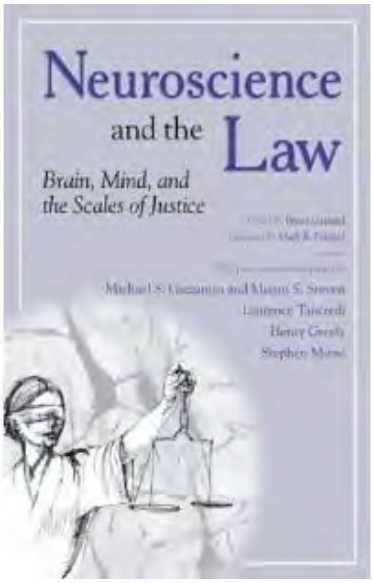
ethics integration in neuroscience

- 研究生活の最初から倫理問題との交流を
- 倫理を配慮する組織的対応
- 研究の構築の際に倫理的要素を不可欠とする
- 研究倫理に関するコンサルテーション・サービス
- 倫理的要素への利害関係者の参加
- 研究チーム自体に倫理の専門家を入れる

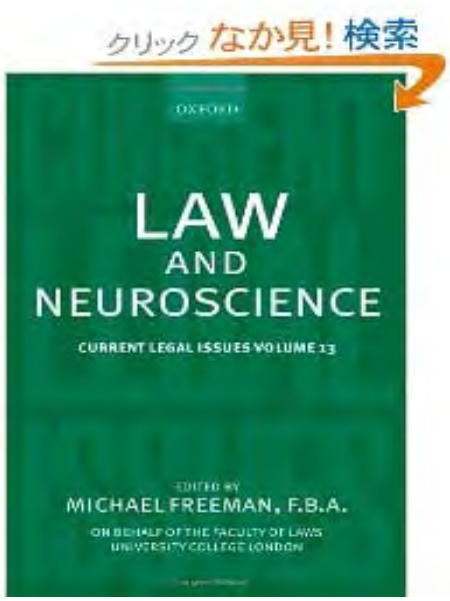
- 勧告
- 脳神経科学の研究には当初から倫理的配慮がなされるべきであり、科学と倫理が相補う関係が望ましい

脳科学と倫理と法—神経倫理学入門
ブレント ガーランド Brent Garland , 古谷 和仁・久村 典子(訳)
みすず書房 (2007/07)

Neuroscience and the Law: Brain, Mind, and the Scales of Justice : A Report on an Invitational Meeting Convened by the American Association for the Advancement of Science Dana Pr; 2nd版 (2004/9/30)
Mark S. Frankel (はしがき), Brent Garland



Law and Neuroscience (Current Legal Issues)
Michael Freeman (編集)Oxford Univ Pr (Sd); 1版 (2011/4/8)



脳科学の発展が法にどのような影響を与えるか

脳科学の発展に法はどのようなスタンスで臨むべきか

脳神経科学と倫理と法
—これらの検討からのヒント

「BMI倫理4原則の提案」。川人光男・佐倉統「BMI倫理4原則の提案」現代化学2010年6月号（471号）21-25頁

1　戦争や犯罪にBMIを利用してはならない

2　何人も本人の意思に反してBMI技術で心を読まれてはいけない

3　何人も本人の意思に反してBMI技術で心を制御されてはいけない

4　BMI技術は，その効用が危険とコストを上回り，それを使用者が確認するときのみ利用されるべきである

→これら4つの原則はあまりに基本的すぎるように見える。

→生命倫理4原則との比較

樋口『ケーススタディ生命倫理と法』（第2 版，有斐閣　2012)

さまざまな法的課題

- １　差別問題
- 　　脳科学による診断による差別
- 　　脳科学へのアクセスに関する差別
- ２　プライバシー
- 　　脳科学→意識下の情報まで収集可能
- 　　非侵襲的装置の開発→空港のセキュリティなど

３　訴訟での利用

　　証言の信用性　黙秘権との関係

４　刑法→犯罪要件としての故意　脳の病？

　　精神的損害の測定可能性

Wilson v. Corestaff Services, 2010 WL 1 949095, at 3 (N.Y. Sup. Ct., May 14, 2010).

United States v. Semrau, Report and Recommendation, No. 07-10074, 2010 U.S. Dist. (W.D. Tenn., May 31, 2010), 2011 WL 9258.

証言の信用力を補強する証拠としての脳神経科学検査（結論としては現段階では否定）

　樋口、前掲書で紹介あり

脳科学研究の進め方（プロセス）

誰が
いかなる方法で
利用目的によって区別可能か

遺伝子研究、再生医療研究との比較
国際的な規制のあり方との比較